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SUPREME COURT OF THE UNITED STATES

OCTOBER TERM, 1958

No. ~~195~~ 27

**MARION B. FOLSOM, SECRETARY OF HEALTH,
EDUCATION AND WELFARE, PETITIONER,**

VS.

**FLORIDA CITRUS EXCHANGE, FRANK R. SCHELL,
ET AL.**

**ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS
FOR THE FIFTH CIRCUIT**

PETITION FOR CERTIORARI FILED JANUARY 2, 1958

CERTIORARI GRANTED MARCH 17, 1958

SUPREME COURT OF THE UNITED STATES

OCTOBER TERM, 1957

No. 703

MARION B. FOLSOM, SECRETARY OF HEALTH,
EDUCATION AND WELFARE, PETITIONER,

vs.

FLORIDA CITRUS EXCHANGE, FRANK R. SCHELL,
ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS
FOR THE FIFTH CIRCUIT

INDEX

	Original	Print
Proceedings in the U.S.C.A. for the Fifth Circuit	a	1
Caption	a	1
Petition for review by Florida Citrus Exchange, case No. 15934	13	2
Petition for stay of order of the Secretary of Health, Education and Welfare	26	10
Exhibit "A"—Letter from George P. Larriek, Commissioner of Food and Drugs to the Honorable James A. Haley, dated February 8, 1955	37	18
Clerk's note re—Final order of Secretary of Health, Education and Welfare	38	19
Affidavit of R. D. Gerwe	38	19
Clerk's note re—Analysis of Dr. R. D. Gerwe, Research Department, FM&CC	41	21
Petition for review by Frank R. Schell, case No. 15948 ..	47	21

	Original	Print
Proceedings before Department of Health, Education and Welfare Food and Drug Administration	52	37
Notice of hearing to amend regulations	52	37
Notice of proposed rule making	53	39
Statement of Chase & Company and Randall Chase	57	47
Exceptions of Coal-Tar Color Industry Committee	82	65
Exceptions of Florida and Texas Users, etc.	158	81
Appendix "A"	165	86
Exhibit 4—Dr. Vos Toxicity tests on FD&C red No. 32	165	86
Brief of interested users, etc.	168	88
Supplemental "A-1"—Report by R. D. Gerwe of the Research Department, FM&CC	203	112
Letter from the Mutual Orange Distributors to Oveta Culp Hobby, dated March 4, 1955	208	116
Petition to reopen by Frank R. Schell	209	116
Exceptions to order and brief on exceptions	214	120
Foreword	214	120
Exceptions to proposed order and to findings of fact	233	134
Brief	234	134
Petition to reopen by Certified Color Industry Committee	259	152
Exhibit "A"—Use of coal-tar colors FD&C orange No. 1, FD&C orange No. 2 and FD&C red No. 32 in finished foods under normal conditions of use	261	153
Order denying petition of the Certified Color Industry Committee to reopen hearing	262	154
Final order of the Secretary of Health, Education and Welfare	281	158
Minute entry of argument and submission, case No. 15934 (omitted in printing)	284	
Minute entry of argument and submission, case No. 15948 (omitted in printing)	285	
Opinion, Jones, J.	286	168
Dissenting opinion, Hutcheson, J.	310	187
Judgment in case No. 15934	315	191
Judgment in case No. 15948	316	191
Order denying petition for rehearing in case Nos. 15934 and 15948	331	192
Clerk's certificate (omitted in printing)	332	
Joint appendix to petitioners' briefs and to respondent's brief consisting of proceedings before the Secretary, Department of Health, Education, and Welfare	336	193
Explanatory note	336	193
Transcript of hearing (excerpts from)	338	194
Preliminary statement of presiding officer, Leonard D. Hardy	338	194

Joint appendix to petitioners' briefs, and to respondent's
brief consisting of proceedings before the Secretary,
Department of Health, Education, and Welfare—Con-
tinued

Transcript of hearing (excerpts from)—Continued		Original	Print
Testimony of Bert J. Vos—			
Direct		341	196
Offer in evidence		352	205
Testimony of Bert J. Vos (continued)—			
Direct		352	205
Cross		363	213
Recross		368	217
Redirect		371	219
Testimony of Edwin L. Gustus		374	221
Cross		378	224
Testimony of Robert C. Evans		378	224
Testimony of Louis Gardner MacDowell—			
Direct		379	225
Testimony of C. Boyd Shaffer—			
Direct		380	226
Exhibit "3"—Chronic toxicity of FD&C orange No. 2, etc.		384	228
Exhibit "4"—Chronic toxicity of FD&C red No. 32, etc.		400	239
Exhibit "8"—Summary table on the concentration of dye on color-added oranges and in products made from color-added oranges		429	259
Clerk's certificate	(omitted in printing)	429a	
Order extending time to file petition for writ of certiorari		430	260
Order allowing certiorari		432	260

[fol. a]

**IN UNITED STATES COURT OF APPEALS, FIFTH
JUDICIAL CIRCUIT**

Pleas and Proceedings had and done at a regular term of the United States Court of Appeals for the Fifth Circuit, begun on the first Monday in October, A. D., 1956, before the Honorable Joseph C. Hutcheson, Jr., Chief Judge, the Honorable Warren L. Jones and the Honorable John R. Brown, Circuit Judges:

No. 15934

FLORIDA CITRUS EXCHANGE et al., Petitioners,

vs.

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare, Respondent

and

No. 15948

FRANK R. SCHELL, Petitioner,

vs.

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare, Respondent

Be It Remembered, That heretofore to-wit, on the 21st day of August, A. D., 1956, a consolidated transcript of the record in the above styled causes, pursuant to petitions for review of orders of the secretary of Health, Education and Welfare was filed in the office of the Clerk of the said United States Court of Appeals for the Fifth Circuit, in Volumes I & II; the petition for review in cause 15934 was filed and docketed on February 2, 1956, and the petition for review in cause 15948 was filed and docketed on February 8, 1956, as follows, to-wit:

[fols. 1-13] IN THE UNITED STATES COURT OF APPEALS FOR
THE FIFTH CIRCUIT

No. 15934

FLORIDA CITRUS EXCHANGE, et al., Petitioners on Review,

vs.

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare, Respondent on Review

PETITION OF FLORIDA CITRUS EXCHANGE AND OTHERS FOR
JUDICIAL REVIEW OF AN ORDER OF THE SECRETARY OF
HEALTH, EDUCATION AND WELFARE, DATED NOVEMBER 10,
1955, F. R. DOC. 55-9209—Filed November 15, 1955

U. S. Court of Appeals, Filed February 2, 1956, John A.
Feehan, Jr., Clerk.

[fols. 14-15] To the Honorable Judges of the United States
Court of Appeals for the Fifth Circuit:

Florida Citrus Exchange, a cooperative under the laws
of the State of Florida, embracing a membership of forty-
four packing houses; Haines City Citrus Growers Associa-
tion, a cooperative under the laws of the State of Florida;
Waverly Growers Cooperative, a cooperative under the
laws of the State of Florida; Herman J. Heidrich, Paul D.
Heidrich and Francis X. Heidrich, a co-partnership doing
business as Herman J. Heidrich & Sons, residents of and
having their principal place of business in Florida; Snively
Groves, Inc., a corporation under the laws of the State of
Florida; Donna Fruit Company, a corporation under the
laws of the State of Texas; J. Floyd Hetrick and Harlow
C. Richardson, a co-partnership doing business as Hetrick
& Richardson; Horace Etchison, Foy G. Hall and Joseph
M. Alex, a co-partnership doing business as McAllen Fruit
and Vegetable Company, Roy Weir, Mrs. I. M. Weir and
J. H. Williams, a co-partnership doing business as Valley
Fruit Company, all being residents of and having their
principal place of business in the State of Texas, present
this petition for Judicial review of an order entered by the

Secretary of Health, Education and Welfare and, in support thereof, respectfully represent as follows:

I

The Nature of the Proceedings

The corporations, cooperatives, associations, partnerships and individuals named in the preceding paragraph, and hereinafter referred to as Petitioners, seek Judicial review of an order of the Secretary of Health, Education [fol. 16] and Welfare, dated November 10, 1955 (F. R. Doc. 55-9209, filed November 15, 1955) and published in the Federal Register under date of November 16, 1955, pages 8492-8495, both inclusive, with the heading,

Title 21—Food and Drugs Chapter 1—Food and Drug Administration, Department of Health, Education and Welfare.

Part 135—Color Certification.

Miscellaneous Amendments.

This order was entered by the Secretary of Health, Education and Welfare under the provisions of the Act of June 25, 1938 (a) 675 paragraph 406, 52 stat. 1049, reorg. plan No. IV, par. 12 effective June 30, 1940, 5 F.R. 2422, 54 stat. 1237, 21 U. S. Code An. Sub-paragraph 346 (b) provides:

“The Secretary shall promulgate regulations providing for the listing of coal-tar colors which are harmless and suitable for use in food and for the certification of batches of such colors, with or without harmless diluents Title 21 USCA page 209.

Petitioners filed their exceptions and briefs in opposition to the order. The order deleted FD&C Red #32 and the action affecting these petitioners appears in paragraph 5 of the conclusions.

II

Jurisdiction of the Court

The Court has jurisdiction by virtue of the Federal Food, Drug and Cosmetic Act (Public Law 717—75th Congress, Chapter 675—3rd session) Act of June 25, 1938, 52 Stat. 1055 and amendments thereto, 21 U.S.C.A. 371,

and the Administrative Procedure Act, Act of June 11, 1946, 60 stat. 243, title 5 U.S.C.A. 1009.

[fol. 17]

III

Facts and Statutes Upon Which Jurisdiction is Based

1. All these petitioners who are natural persons reside in the Fifth Circuit; all those who are partnerships are residents of and have their principal place of business in the Fifth Circuit; and all those that are corporations have their places of business in the Fifth Circuit.

2. An actual controversy exists as to the validity of the order hereinbefore and hereinafter referred to and all these petitioners will be adversely affected by such order if placed in effect and all of them are adversely affected and aggrieved by the action of such agency entering the order and all are entitled to have the order reviewed by judicial review under the statute referred to in Paragraph II.

3. Your petitioners are engaged in the packing and marketing of oranges, and some are also growers of oranges, some in the State of Florida and some in the State of Texas; they are all users of dye FD&C Red No. 32 for the coloring of oranges and have been such users for many years; that they, together with many others similarly situated, have large sums of money invested in the equipment for the coloring of oranges with FD&C dye Red No. 32 and that such dye has been in common usage for the coloring of oranges since before 1938.

4. That the United States Department of Agriculture recognizing that oranges mature and fully ripe, still remained [fol. 18] green on the outside encouraged and approved the coloring of fully mature oranges and over the years a market has been developed whereby the public buys the colored oranges much more readily than it would those greenish in color even though fully mature.

5. That in 1939 the Department of Agriculture, which Department had at that time jurisdiction of the Food, Drug and Cosmetic Act, after extensive studies and hearing certified FD&C Red No. 32 as "harmless and suitable for use in the coloring of foods", and since that time more than 59 per cent of all the oranges shipped in Florida and a large percent in Texas have been colored with said dye;

that FD&C Red No. 32 is now used solely for the coloring of oranges and that there is no other certified color available.

6. That the laws of both Florida and Texas have been standards requiring maturity before shipment; that the laws of the State of Florida only allows coloring upon oranges that have greater standards of maturity than uncolored oranges; that oranges must meet the U. S. and State standards as to grade and pack and such color cannot be used to cover inferiority; that the coloring matter FD&C Red #32 is harmless and is particularly adapted to the coloring of oranges and is not harmful in the manner and quantity used; that the effect of the order would be to demoralize the orange market, to greatly reduce prices, to disrupt trade practices that have been in existence for many years and in many instances make it practically impossible to sell oranges because the public has been educated to buy oranges with an orange coloring, and would [fol. 19] result in irreparable injury and get financial loss to these petitioners and the orange growers of Florida and Texas impossible to measure in dollars and cents, that at certain seasons of the year it is practically impossible to sell uncolored oranges because the orange is one of the very few fruits that has blossoms, small fruit and fully ripe and mature fruit on the tree at the same time, that when the chlorophyll (green color) rises in the tree to go into the leaves and new fruit it likewise goes into the mature and ripe fruit "regreening" it, causing it to be green on the outside when it is mature, and by reason of this it is practically impossible to sell unless colored. This caused the Industry and the United States Department of Agriculture to spend vast sums in research. The color method using FD&C Red #32 was developed, approved and certified as "harmless and suitable for use in food" and at the time of the hearing had been used in coloring of more than two hundred and fifty six million boxes of oranges, and since the hearing additional to bring the total to in the neighborhood of three hundred million boxes being more than half or all fresh oranges shipped and in some areas and in some of the petitioners packing house 100% of all oranges shipped are so colored, without any harmful effects to any human.

7. The order will deny to petitioners the use of the only dye now available for use in the coloring of oranges, which is the color that has been certified for 17 years.

The Order was entered and published in the Federal Register under date of November 16th, 1955, and will take effect 90 days from that date (February 14, 1956), unless stayed or suspended by this Honorable Court.

[fol. 20]

IV

Points on Which Petitioners Intend to Rely

In this petition for Judicial review of the order insofar as it relates to FD&C Red #32, petitioners intend to rely on the following points among others:

1. The order is illegal and erroneous and based upon the Secretary's erroneous construction of the law, taking the position that there must be zero toxicity and that a coal-tar color containing a harmful ingredient is per se harmful and not harmless notwithstanding the quantity and manner of use. This interpretation is contrary to the construction of the word "harmless" as intended in the passage of the Act, the record showing that only four parts per million of coloring matter applied on the outer rind, not even penetrating the rag, and that juice extracted from color-added oranges contains only 0.07 parts per million of coloring matter, whereas the Congressional hearings the then head of the Food, Drug and Cosmetic Department sponsoring the legislation informed the Committee in the House of Representatives:

"There are very few things in which you will not find contaminating products in some degree."

The Senate hearings show the toxic contents of fish, cod-liver oil and other named foods far in excess of the coloring matter applied to oranges and that the toxic ingredients in shrimp and prawn were 30 parts per million (7½ times all the coloring matter on an orange and more than 420 [fol. 21] times the amount of coloring matter found in the juice extracted from color-added oranges.)

2. The order is arbitrary and illegal because the tests and the findings on which same are based are unrealistic and have no relation to the methods and manner in which

FD&C Red #32 is used on oranges. The report showed no adverse effect when fed at the lowest level selected for that purpose and these levels were in excess of the amount of color likely to be ingested under normal usage.

3. The order and the findings on which it is based are erroneous and arbitrary in that they did not take into consideration the use to which the color is to be used and the record showing that in the ratio of the amounts fed to rats and dogs as compared to human beings it is not harmful to human beings and is not harmful in the manner and quantity in which it is used.

4. The order is arbitrary and unlawful because it ignores the undisputed testimony in the record that the amount of dye and the amount and method of proposed use was necessary to determine whether it was harmless. This method of testing and evaluating was not followed even though the record shows that FD&C Red #32 is only used for the coloring of oranges, that it is the only color certified for use used for coloring oranges and that it is harmless in the manner and quantity it is used, and that the legislative history of the Act show- that it was known and intended in the passage of the Act that coal-tar colors were to be used in the coloring of oranges.

[fol. 22] 5. The record contains no substantial evidence to warrant the order deleting Dye FD&C Red #32 for the coloring of food and particularly the coloring of oranges.

6. The Order ignores the record which shows that there is no data as to whether the color is or is not harmless for external application and ignores the record which shows affirmatively that FD&C Red #32 in the manner and quantity applied to oranges has no harmful effects. And the order is arbitrary, unlawful and capricious in that it construes the word "harmless" in an unreasonable manner and contrary to that intended by Congress in the passage of the Federal Food, Drug and Cosmetic Act.

7. The order is based on an unrealistic test, the feeding to the test animals was many times that which would be ingested by man under normal usage or under any reasonable condition or in the manner and quantity in which the color is used.

8. The Order is not based on the whole record and erroneously disregards substantial evidence of record.

9. The Secretary has mis-interpreted the law and erroneously takes the position that if there is any harmful ingredient in the coal-tar color that it is not harmless and cannot continue to be certified even though the record shows and it is admitted that it is harmless in the manner and quantity as used in the coloring of oranges. This is an arbitrary and strained construction and not a reasonable construction and ignores the decision of the United States Supreme Court in the case of Lexington Mill and Elevator Co. 232 U. S. 339, 58 Law Ed. 658 wherein The Court said: [fol. 23] "In recognizing that small quantities of arsenic is not injurious to health, the government acknowledges that this term is a relative one. Arsenic is found in infinitesimal quantities in so many articles of food that it has been said that the air we breathe, the water we drink, the smoke and dust we inhale, and all the foods we consume contain arsenic. If the terms be an absolute one, then they would all be condemned. The quantity of arsenic found in this color material is so infinitesimal that, when diluted as it is ordinarily used, it would take years to produce 'a dose' such as is ordinarily prescribed by physicians—one-thirtieth of a grain. In other words, one would be required to drink 150,000 bottles of soda before he would have consumed a quantity of arsenic sufficient to equal the 'dose'...."

10. The Order is erroneous for the reason that the record affirmatively shows that the tests were made upon two ingredients and that it is not shown that they were of satisfactory purity as to freedom from harmful substances when they were received or tested. It not being shown even that the ingredients were received from commercial firms ordinarily engaged in preparing FD&C Red #32.

11. The Order and the findings are not based upon substantial testimony, and are arbitrary, capricious and in excess of the Secretary's power under the law, and illegal for other reasons apparent upon a review of the record.

12. The Order takes an erroneous construction of the law, taking the position that the Secretary cannot certify for restricted use in coloring foods and based on the erroneous belief that the color must be harmless when used in all goods. This is contrary to the law and contrary to the basic concept on which the color was certified. The

record of that hearing shows the position of the Chief of the Pharmacology Division F.D.A. When FD&Red #32 was certified in 1939 (21 CFR 135.3) as harmless and suitable for use in food, his statement being:

(Dr. Calvery.) "No, in my opinion there are no coal-tar colors that are harmless and suitable for use in all kinds and classes of Foods, Drugs and Cosmetics. . ."

"Yes, by harmless and suitable for use for purposes indicated, we mean that in the concentrations that these substances are used for coloring purposes, it is our opinion that no harm can come from them to the user when used in the concentrations for which they are designed and for the purposes for which they are designed. . ."

(U.S.D.A.—FD & C #4, Feb. 7, 1939, page 228)

V

Prayer for Relief

Wherefore, Petitioners hereinbefore named cause this Petition to be signed in their behalf by their undersigned attorney and petitioners respectfully pray that this Honorable Court grant a review of the proceedings resulting in the order of the Secretary of Health, Education and Welfare, dated November 10, 1955 as hereinbefore referred to and the order itself; that a copy of this Petition and the [fol. 25] Petition for Stay be transmitted to the Secretary of Health, Education and Welfare of the United States; and that the Secretary be required to certify and file with this Court a transcript of the record upon which the said order was entered as required by law; and that upon such review the above described order be set aside insofar as it relates to FD&C Red #32 and held for naught; that this Court enter an order setting aside temporarily and staying the taking effect of the order of the Secretary of Health, Education and Welfare insofar as it relates to the use of FD&C Red #32, until the final determination of the petition for review in this case; that this Honorable Court enter a stay order, injunction or any and all necessary and appropriate process to postpone the effective date of the Secretary's order insofar as it relates to FD&C Red #32 and to preserve status or rights of these petitioners

pending conclusion of the review proceedings, or; if the Court in its discretion, should determine that the relief prayed for hereinbefore should not apply to the entire order insofar as it affects FD&C Red #32, then petitioners pray that the Honorable Court grant a stay order or other orders staying the operation of the Secretary's order insofar as it relates to the use of FD&C Red #32 for the coloring of mature oranges, when harmless in the manner and quantity as used; and that Petitioners may have such other and further relief as the allegations herein may warrant and as to the Court may seem meet and proper.

Dated January 30, 1956.

(S.) J. Hardin Peterson, Attorney for Petitioners
on Review.

Cochrane Building, Lakeland, Florida.

[fol. 26] IN THE UNITED STATES COURT OF APPEALS FOR THE
FIFTH CIRCUIT

No. —

FLORIDA CITRUS EXCHANGE, et al., Petitioners on Review,

vs. —

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare, Respondent on Review.

PETITION FOR STAY OF ORDER OF THE SECRETARY OF HEALTH,
EDUCATION AND WELFARE—Dated January 30, 1956.

To the Honorable Judges of the United States Court of
Appeals for the Fifth Circuit:

Florida Citrus Exchange, a cooperative under the laws of the State of Florida, embracing a membership of forty-four packing houses; Haines, City Citrus Growers Association, a cooperative under the laws of the State of Florida; Waverly Growers Cooperative, a cooperative under the laws of the State of Florida; Herman J. Heidrich, Paul D.

Heidrich and Francis X. Heidrich, a co-partnership doing business at Herman J. Heidrich & Sons, residents of and having their principal place of business in Florida; Snively Groves, Inc., a corporation under the laws of the State of Florida; Donna Fruit Company, a corporation under the laws of the State of Texas; J. Floyd Hetrick and Harlow C. Richardson, a co-partnership doing business at Hetrick & Richardson, Horace Etchison, Foy G. Hall and Joseph M. Alex, a co-partnership doing business as McAllen Fruit and Vegetable Company, Roy Weir, Mrs. I. M. Weir and J. H. Williams, a co-partnership doing business as Valley [fol. 27] Fruit Company, all being residents of and having their principal place of business in the State of Texas, hereinafter referred to as Petitioners, who are concurrently filing with the Court a Petition in the above entitled cause for Judicial review of an order dated November 10, 1955 and to become effective on the 14th day of February, 1956, present this Petition to stay the order of the Secretary referred to above pending Judicial review and in support of this petition respectfully represent and allege the following:

I

The Petition for Judicial Review

The Petition for Judicial Review filed concurrently with this petition is incorporated in this petition by reference. The Court is respectfully urged to read the Petition for Judicial Review and before reaching a conclusion on this petition for a stay order.

— II

The Applicable Statutes

Sec. 70 (f) (3) Federal Food, Drug and Cosmetic Act (Act of June 25, 1938, 52 Stat 1056, 21 U.S.C.A. Par 371, (f) (3), page 238 provides as follows:

“The Court shall have jurisdiction to affirm the order or to set it aside in whole or in part, temporarily or permanently.”

The Administrative Procedure Act, Act of June 11, 1946, 60 Stat 243, title 5, par. 1009 U.S.C.A. appearing as part of

[fol. 28] subparagraph (d) of par. 1009 page 464 U.S.C.A. Provides as follows:

"Upon such conditions as may be required and to the extent necessary to prevent irreparable injury, every reviewing Court (including every Court to which a case may be taken on appeal from or upon application for certiorari or other writ to a reviewing Court) is authorized to issue all necessary and appropriate process to postpone the effective date of any agency action or to preserve status or rights pending conclusion of the review proceedings."

III

Statement of Cause

The petitioners respectfully refer to their petition for review as part of the cause is recited therein and, in addition thereto would show as follows:

That the Food, Drug and Cosmetic Act required the certification of coal-tar colors that were "harmless and suitable for use in food", that pursuant to that authority coal-tar dye designated as FD&C #32, which has been temporarily certified and which had been used prior to the permanent certification was certified in 1939 as "harmless and suitable for use in food" (21 CFR 153.3); that petitioners are the operators of packing houses packing oranges and a number of them are growers of oranges and all now use and have been using said color for a number of years. Petitioners ship several million boxes of color-added in bringing this suit, and that the packers using this color for oranges and packing more than 88 per cent of the [fol. 29] oranges so colored, joined in the exceptions to the Secretary's order and it is only for convenience that they are not named herein. These petitioners, pack a number of million boxes each year and it is necessary to color with this color a high percentage of the oranges shipped by them, some of these petitioners having to color all of the oranges shipped by them with the use of this color and all of the shippers coloring a substantial amount.

That under date of November 10, 1955, Secretary of Health, Education and Welfare entered an order deleting this color from the certified list. This is the only

color certified for the coloring of oranges and when color added is referred to herein it means FD&C Red #32.

This order will result in irreparable injury to petitioners and each and all of them and denies to them the only dye now certified and suitable for use in coloring oranges and the purpose of this proceeding is to stay the taking effect of the Order of the Secretary until the final determination of the Petition for review by the Court.

IV

Reasons in Support of a Stay Pending Judicial Review

The Secretary's Order will go into effect on February 14, 1956 unless it is stayed. Unless it is stayed irreparable injuries will result to the petitioners and each and every one of them, some details of which are hereinabove set [fol. 30] forth; that the granting of the stay will not be against the public interest and will not affect the public health but will result in keeping the status quo of the matter as it has been for around 17 years without any injury to the public.

The Department of Health, Education and Welfare does not take the position that the use of this color is harmful when used in the coloring of oranges but takes the position that only harmless colors are eligible for certification and that the FD&C Red #32 cannot continue to be certified for use though it is admitted that it is harmless in the manner and quantity in which it is used in the coloring of oranges.

In a letter dated February 7, 1955 when the question of decertification was pending the Commissioner of the Food and Drug Administration, George P. Larrick, advised officially:

"There is, however, no evidence that in the amounts used and in the manner of use, in the coloring of citrus fruit the product so colored is not safe for human consumption."

(Letters to Honorable Spessard L. Hollard, U.S. Senator, Honorable George E. Smathers, U.S. Senator, and Honorable James A. Haley, Member of Congress), copy

of one of these letters attached as exhibit A and made a part hereof.

That it is necessary in order to market certain varieties of early oranges and certain varieties of late oranges that they are colored. The Department of Agriculture has long recognized this and as early as 1932 in the [fol. 31] U.S. Department of Agriculture annual report, excerpts from which were filed in the hearings on the Food, Drug and Cosmetic Act in 1935, and the Department of Agriculture Year Book for 1932, pages 134 to 137 states:

"Some of the early fall varieties of oranges and grapefruit ripen while the fruit is still green in color. Later varieties that mature in the spring or summer assume the color of full maturity during the winter while the fruit is still immature, but when warm spring weather occurs the rind may turn green again. Thus, while the edible part of the fruit ripens there is a 'regreening' of the rind. . ."

"Grapefruit growing inside densely foliated trees never develops full color, although some of the best-flavored fruit is produced there. There is, therefore, no definite relation between flavor or maturity and the color of the fruit while on the tree. However, there is a very significant relation between the color of the fruit offered for sale and the price that it will bring, and citrus fruit producers have always faced the problem of making the color of ripe fruit match its flavor."

Excerpts from U. S. Department of Agriculture Bulletin 1159 filed in hearings on Food and Drug Legislation (Hearings H of R 1935 pp. 172-189) had this to say:

"It is well known that citrus fruits grown under certain climatic and cultural conditions may be mature and highly desirable for food while the skin of the fruit is still green in color. . ."

[fol. 32] "On the other hand, green-colored fruit, no matter what the quality, is difficult to merchandise. In the mind of the consuming public a green-colored orange is immature and unfit for food. The public desires fruit for decorative purposes as well as for eating, and a well-

colored orange is much more attractive than one green or partially green in color. It is evident, then, that some method of treating this fruit so that it would assume a rich orange yellow color early in the season, when it is most desirable for food, would be of benefit to the industry and to the consuming public alike."

Under the State law color is only allowed upon mature oranges and in Florida a greater standard is required for coloring than for other oranges. It is necessary to color in order to sell at a fair price. The late variety of oranges are already beginning to re-green as the Spring growth comes into the tree and it would be impossible to sell many of the Valencias at any price at all or others at vastly reduced prices unless they are colored. This will result in the loss of many millions of dollars to the petitioners and many other growers and packers similarly situated and will cause unemployment to those engaged in the picking and packing of fruit and will cause irreparable injury impossible to measure in dollars and cents to these petitioners and each of them. To stay the order would not be detrimental to the public interest. Around three hundred million boxes of color-added oranges have been shipped without injury to human beings. This is around 59% of all oranges shipped since the certification of the dye. The amount used of coloring matter is very minute, only 4 parts per million applied on the outside of the rind. This is less than the toxic [fol. 33] matter contained naturally in shrimp, prawn, cod liver oil, fish, and a number of other foods. The dye is oil soluble and does not even penetrate the rag of the orange. No harm would result in the granting of the stay and great and irreparable injury would result to petitioners and to many other if the Order delisting FD&C Red #32 takes effect.

V.

Prayer for Relief

Wherefore, Petitioners hereinbefore named cause this Petition to be signed in their behalf by their undersigned attorney and petitioners respectfully pray that this Court

enter an order setting aside temporarily and staying the taking effect of the order of the Secretary of Health, Education and Welfare insofar as it relates to the use of FD&C Red #32, until the final determination of the petition for review in this case; that this Honorable Court enter a stay order, injunction or any and all necessary and appropriate process to postpone the effective date of the Secretary's order insofar as it relates to FD&C Red #32 and to preserve status or rights of these petitioners pending conclusion of the review proceedings, or: if the Court in its discretion, should determine that the relief prayed for hereinbefore should not apply to the entire order insofar as it affects FD&C Red #32, then petitioners pray that the Honorable Court grant a stay order or other orders staying the operation of the Secretary's order insofar as it relates to the use of FD&C Red #32 for the coloring of mature oranges, when harmless in the manner and quantity as used; and that Petitioners may have such other [fol. 34] and further relief as the allegations herein may warrant and as to the Court may see meet and proper.

Petitioners have appended hereto a copy of the Order and Exhibit "A".

Dated January 30, 1956.

J. Hardin Peterson, Attorney for Petitioners on Review.

Cochrane Building, Lakeland, Florida.

AFFIDAVIT

STATE OF FLORIDA,
County of Polk:

Personally appeared before me, J. Hardin Peterson, who being duly sworn deposes and says:

That he is attorney for petitioners in the above cause and that he prepared and read the foregoing petition and that the allegations contained therein are true; that in addition to being attorney as aforesaid that he is an orange grower, and has been for 30 years or more and served as attorney for the Florida State Department of Agriculture; that he is attorney for a large segment of citrus packing houses, that he has followed the problem of coloring

oranges for many years and is familiar with the problem; that based upon his knowledge and experience that the putting into effect of the Order of the Secretary would cause irreparable loss to petitioners and would be an impact on the citrus industry that would cause great and [fol. 35] vast loss to many others; that the petition is filed in good faith.

J. Hardin Peterson.

Sworn to and subscribed to before me this 30th day of January, 1956.

Frances M. Linsner, Notary Public, State of Florida.
(Seal.)

My commission Expires: April 4, 1959. Bonded by American Surety Co. of N. Y.

CERTIFICATE OF SERVICE (omitted in printing)

AFFIDAVITS AS TO PETITIONS

STATE OF FLORIDA,
County of Polk:

Personally appeared before me John A. Snively, who, being duly sworn, deposes and says that he is President of Snively Groves, Inc. and that the allegations in the Petition for Review hereinbefore set forth are true, and that said Petition is filed in good faith.

(S.) John A. Snively.

[fol. 36] Sworn to and subscribed to before me this 31st day of January, A. D. 1956.

(S.) Ruby Snead, Notary Public, State of Florida
At Large.

My Commission Expires: March 23, 1957.

STATE OF FLORIDA,
County of Polk:

Personally appeared before me, John A. Snively who, being duly sworn, deposes and says that he is President of Snively Groves, Inc., one of the Petitioners in the foregoing

petition for stay and that the allegations of said petition for stay are true; that this company has shipped many millions of boxes of oranges using FD&C Red #32 for coloring, without any harmful effects and that it is at present a user thereof, and that to deny the use of this dye will make it practically impossible to market oranges without coloring and will result in great loss, impossible to definitely measure in dollars and cents and will result in irreparable injury to this Petitioner and many others..

(S.) John A. Snively.

Sworn to and subscribed before me this 31st day of January, A. D. 1956.

(S.) Ruby Snead, Notary Public, State of Florida
At Large.

My Commission expires: March 23, 1957.

[fol. 37] IN UNITED STATES COURT OF APPEALS

EXHIBIT "A" TO PETITION

Department of Health, Education, and Welfare, Food and
Drug Administration, Washington 25, D. C.

Feb. 8, 1955.

Honorable James A. Haley, U. S. House of Representatives,

DEAR CONGRESSMAN HALEY:

In response to your request we have prepared this statement with regard to the coloring of citrus fruit.

As is stated in the enclosed reprint from the Federal Register of December 30, 1954, we recently proposed the amendment of the Color Certification Regulations to delete the colors designated as FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32. The date for receiving objections and comments on the proposal has been extended to include March 7, 1955. No final action will be taken on this proposal until some time after that date. The proposal is based upon evidence adduced at a recent hearing

which indicates that these colors are not harmless for use in food within the meaning of Section 406 of the Federal Food, Drug, and Cosmetic Act, as was previously believed.

Pending our further consideration of this matter and the final determination thereon and the issuance of new color certification regulations, no ban is placed on the use by the citrus industry of the colors designated above or on the sale and shipment of color-added citrus fruit.

FD&C Red No. 32 is the color that has been generally used in the coloring of oranges.

[fol. 38] The proposal to remove these coal-tar colors, including FD&C Red No. 32, from the list of colors eligible for certification for use in food results from the requirement of the Pure Food Law that only colors that are harmless are eligible for certification. Recent investigations show that these colors when fed in substantial amounts, show evidence of toxicity. There is, however, no evidence that, in the amounts used, and in the manner of use, in the coloring of citrus fruit, the product so colored is not safe for human consumption.

Sincerely yours, (S.) Geo P. Larrick, Commissioner
of Food and Drugs.

Enclosure.

FR Rep 12-30-54 re color.

Feb. 8, 1955.

Final Order of Secretary of Health, Education and Welfare, dated November 10, 1955 Omitted hereinafter copied at page 158.

AFFIDAVIT

STATE OF NEW YORK,
County of New York:

Personally appeared before me, R. D. Gerwe, who, being duly sworn, deposes and says:

[fol. 39] That he is Head of the Research Department of the Food Machinery and Chemical Corporation; that he has had a broad education and experience in the matter of food, food chemistry and food colors and matters relating

to oranges and the coloring matter used on oranges; that his background of education is as follows:

B. S. Miami University, Oxford, Ohio, 1927.

M. A. University of Cincinnati, 1929.

Ph. D. University of Cincinnati, 1932.

Instructor in Chemistry, Oxford College, Oxford, Ohio, 1927-28.

Research Chemist, University of Cincinnati, 1928.

Graduate Assistant Instructor, Univ. of Cincinnati, 1928-32.

John Uri Lloyd Fellow at Univ. of Cincinnati, 1930-32.

Part time employment as Research Chemist by William S. Merrell Company of Cincinnati, 1929-30.

Employed by Kroger Food Foundation and Kroger Company in charge of Research and Development Department, 1932-38.

Employed by Food Machinery and Chemical Corporation, Lakeland, Florida, as Director of Research, 1938—

[fol. 40] That he made the study and analysis as shown on the two sheets attached hereto and which are made a part of this affidavit the same as if incorporated therein; and that it is a fair, scientific and correct analysis based upon scientific formulae and data as set forth therein.

That FD&C Red #32 is an oil soluble color used on the outside of oranges and does not penetrate the rag or inside of the orange; that such color has been used in the coloring of oranges since 1939, and to some extent prior thereto; and that more than 256,000,000 boxes had been shipped, colored with this color, at the time of the Food and Drug hearings, and that there was no instance of any detrimental effect to humans.

That the feeding tests used and shown in the testimony were unrealistic and in far greater proportions as to amount than would be ingested by human beings; that FD&C Red #32 is the only color certified for the coloring of oranges; that under any reasonable construction of the word "harmless" FD&C Red #32 is harmless; that the Food and Drug Administration has repeatedly said:

"There is, however, no evidence that, in the amounts used, and in the manner of use, in the coloring of citrus fruit, the product so colored is not safe for human consumption."

That the eating of oranges colored with said color would not be harmful in any way to human beings and that there is no danger to the public or the public health by reason [fol. 41-46] of the continuation of the use of such color.

(S.) R. D. Gerwe.

Sworn to and subscribed before me this 28 day of January, A. D. 1956.

(S.) Frank M. Vento, Notary Public, State of New York. (Seal.)

My commission expires: Mar. 30, 1957. No. 03-4094050.

Qualified in Bronx County. Certified in New York County.

Analysis of Dr. R. D. Gerwe, Research Dept., FM&CC, dated 3*16*54, Omitted hereinafter copied at page 112.

[fol. 47] UNITED STATES CIRCUIT COURT OF APPEALS FOR
THE FIFTH CIRCUIT

No. 15948

FRANK R. SCHELL, Petitioner on Review

vs.

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare, Respondent on Review

PETITION FOR REVIEW—Filed February 8, 1956

J. Lewis Hall, P. O. Box 55, Tallahassee, Florida,
Attorney for Petitioner.

[File endorsement omitted.]

[fol. 47a]. To the Honorable Judges of the United States
Circuit Court of Appeals for the Fifth Circuit:

Frank R. Schell, a citizen of the United States and of
the State of Florida, whose place of business is at 1602.

Richardson Place, Tampa 6, Florida, presents this Petition for judicial review of an order entered by the Secretary of Health, Education and Welfare, dated November 10th, 1955, and, in support thereof, respectfully represents as follows:

I

The Nature of the Proceedings

Your Petitioner seeks a review of an order of the Secretary of Health, Education and Welfare, dated November 10th, 1955 (F.R. Doc. 55-9209, filed November 15, 1955) and published in the Federal Register under date of November 16, 1955, pp. 8492-8495, both inclusive, with the heading:

"Title 21—Food and Drugs

Chapter 1.—Food and Drug Administration, Department of Health, Education and Welfare:

Part 135—Color Certification Miscellaneous Amendment."

This order was entered by the said Secretary, statedly under the provisions of the Act of June 25, 1938, (c) 675, paragraph 406, 52 Stat. 1049; Reorg. Plan No. IV, par. 12, effective June 30, 1940; 5 F.R. 2422, 54 Stat. [fol. 47b] 1237, 21 U.S. Code Ann. Subparagraph 406 (b) of the Act of June 25, 1938, reads:

"The Secretary shall promulgate regulations providing for the listing of coal-tar colors which are harmless and suitable for use in food and for the certification of batches of such colors, with or without harmless diluents." (Title 21 USCA p. 209.)

The above mentioned order deleted the coal-tar food colors designated as FD&C Red No. 32 and FD&C Orange No. 2 from the list of certifiable colors and the action affecting the interests of this Petitioner appears in par. 5 of the conclusions.

Petitioner filed his exceptions and brief in opposition to said order, together with petition to re-open the proceedings and take additional testimony to rectify the omission of pertinent and important matters and things which latter petition was ignored by the said Secretary.

II

Jurisdiction of this Court

The Court has jurisdiction by virtue of the Federal Food, Drug and Cosmetic Act (Public Law 717—75th Congress, Chapter 675—3rd Session) Act of June 25, 1938, 52 Stat. 1055 and amendments thereto (21 U.S.C.A. 371) and the Administrative Procedure Act, Act of June 11, 1946, 60 Stat. 243 (Title 5 U.S.C.A. 1009).

[fol. 47c]

III

FACTS AND STATUTES UPON WHICH JURISDICTION IS BASED

(1) Your petitioner resides and has his place of business within the Fifth Circuit.

(2) An actual controversy exists as to the validity of the order hereinbefore and hereinafter referred to and Petitioner will be adversely affected by such order if placed in effect and is adversely affected and aggrieved by the action of such Agency entering the order and is entitled to have the order reviewed by Judicial review under the Statute referred to in Paragraph II.

(3) Your Petitioner originated and retains an interest in the several patents on what has become known as the Color Added process, being a process for artificially enhancing the varietal color of mature citrus fruits, particularly oranges, by the impregnation of the peel thereof with a certified food color. The food colors FD&C Orange No. 2 and FD&C Red. No. 32, attempted to be deleted by said order, are the only colors adapted or adaptable to such coloration of oranges at this time. Your Petitioner is also a producer of oranges, but derives his principal income from royalties from said Color Added process, which income would be destroyed by said order.

IV

POINTS UPON WHICH PETITIONER WILL RELY

Petitioner herewith presents the points upon which he [fol. 47d] will rely for reversal of the order of the Secretary, such points to be presented in the following order:

1. Nature of "Color Added" Process
2. Necessity for "Color Added"

3. The evidence upon which the order of the Secretary was entered is wholly insufficient
4. The order of the Secretary is unfounded in law.

(1) Nature of the Color Added Process

The Color Added process comprehends the use of a coloring medium comprising an oil-soluble certified food color (FD&C Orange No. 2 or FD&C Red No. 32, both attempted to be banned by the order of November 16, 1955, herein appealed from); a minute amount of solvent for the food colors; soap or another emulsifying and surface tension reducing agent, and water.

The oranges are immersed in this liquid for a period of two to three minutes, or the liquid is poured or sprayed on the oranges for a like period of time. The maximum temperature of the coloring medium is fixed by law at 123° F. The temperature of the inner juice is raised not over 2° F. by this process.

The color is absorbed from the coloring medium by the very thin layer of oily and waxy materials in the extreme outer surface of the peel, which layer is about 1/1000 of an inch thick. The color cannot penetrate beyond this outer layer of oily and waxy material and is chemically incapable of coloring the white cellulosic material of the peel, [fol. 47e] nor can it color the inner membranes (rag) or the juice cells or the juice of the orange.

The peel of an orange thus treated contains *four parts of color per million parts of whole orange*. The juice of an orange so colored contains *7/100 of one part of color per million parts of juice by weight*, that color being held in peel oil that escaped into the juice during extraction of said juice.

It should here be noted that while F&DA is contending for a right to prohibit the use of a color which, for 14 years, it has certified to be "harmless and suitable for use in foods" and which is used at the rate of 4 parts of color per million parts of the whole orange, and has no cumulative properties, F&DA has recently issued, under the provisions of Sub-Section 406 (a) of the 1938 FD&C Act, standards of tolerances for deleterious spray residues permitted to remain on citrus fruits and that these standards prescribe a tolerance of 7 p.p.m. for arsenate of lead, a known deadly

poison of known cumulative effect, being 175% of the peel content of the certified food color FD&C Red. No. 32 or FD&C Orange No. 2.

(2) Necessity for "Color Added"

All citrus producing areas harvest their early varieties while the peel is still green in color, although the fruit is mature by all standards. All areas use ethylene gas (1 cubic foot of gas to 3000 cubic feet of air) to decompose the green chlorophyll in the peel.

In the case of all varieties grown in Florida and Texas the orange thus degreened has a pale, sickly yellow appearance when the green color first disappears, and further [fol. 47f] exposure to the ethylene gas will deepen that color but little. The same is true of all California varieties *except* their Navel orange.

In the case of the California Navel orange, that variety, also, has a pale yellow coloration when the green first disappears, but further exposure to the ethylene gas, for another 24 to 36 hours, deepens that color to a rich, orange-red that is perfect in its eye appeal. A noted plant physiologist, after three years study of the subject, identified this added color as a species of harmless burn (comparable to a mild sunburn of the human skin) resulting from the action of the gas upon some unidentified constituent of the peel of the California Navel orange only.

Since the *natural* color of the California Navel, as disclosed when the green is first blanched out, is that pale, sickly yellow, then the color resulting from such further exposure to ethylene gas is obviously as artificial as that had from the use of "Color Added."

As was said by the Circuit Court of Appeals in *Lexington Mill and Elevator Co. vs. U. S.* (202 Fed 615; aff. U.S.S.C., 232 U.S. 399) where the issue was the propriety of bleaching the yellowish tint from flour:

"The mixture referred to in the first subdivision must be held to include a chemical compound as well as a mechanical mixture. . . . Similarly, the word 'colored' must be held to include any artificially produced change in the natural color of the substance. . . . This is the evident intent of the statute." (Emphasis ours.)

This perfect artificial color gave to the California citrus [fol. 47g] industry a competitive advantage that was well nigh absolute, as is shown by the following figures:

For the shipping season of 1923-24, when the ethylene gas process first went into general use, Florida produced 13,150,000 boxes of oranges, Texas produced 6,000 boxes and California produced 24,153,000 boxes.

For the shipping season of 1934-35, Florida produced 15,600,000 boxes, Texas produced 650,000 boxes and California produced 45,047,000 boxes of oranges.

Florida, struggling against California's monopoly of a perfect artificial color, had increased her production, in eleven years, by only 2,450,000 boxes, and was having great difficulty in marketing even that small production. Texas shipped but little of her crop in interstate commerce. California, however, had increased her production by 20,894,000 boxes, or nearly nine times Florida's increase.

In the shipping season of 1934-35 the Color Added process went into use in Florida and Texas. Even with the handicap of being required to stamp each orange "Color Added," while the artificially colored California Navel carried no declaration of artificial color, the Color Added process largely equalized the monopoly of artificial color theretofore enjoyed by the California industry.

In 1944-45, just ten years later, Florida produced 42,800,000 boxes of oranges, an increase of 27,200,000 boxes; Texas produced 4,400,000 boxes, an increase of 3,750,000 boxes, and California in her best year ever, under very favorable growing conditions, produced 60,500,000 boxes (against 51,961,000 boxes in 1943-44 and 44,010,000 boxes in 1945-46) [fol. 47h] an increase over 1934-35 production of 15,453,000 boxes, largely due to increase in production capacity of older trees and of young trees planted before the impact of Color Added was fully evident.

Florida and Texas production continued to climb, until in 1951-52 Florida was producing 78,600,000 boxes; Texas which had increased to 5,200,000 boxes in 1947-48 before her two disastrous freezes in 1949-50 and 1950-51, was starting over with 300,000 boxes, while California was down to 38,410,000 boxes, a decrease of 22,090,000 boxes.

For the year 1954-55, Florida produced more than

90,000,000 boxes, while California's production was some 40,000,000 boxes.

There is no intent to claim that "Color Added" is due the entire credit for Florida's ability to market her present huge volume of oranges. On the contrary, when, in 1947-48, Florida's production reached 58,400,000 boxes, the peak production for which Color Added is entitled to a substantial part of the credit, we faced definite signs of over-production. But in the meantime the frozen concentrated juice process was coming into full production and picked up the slack, enabling Florida to go on to new production heights.

From 1933 until 1938 F&DA, under the direction of Hon. Walter G. Campbell, Chief, who was fanatically opposed to the use of *any* artificial color on or in any food, beverage, drug or cosmetic, strove to outlaw the Color Added process. That opposition did not cease until [fol. 47i] the Congress, by the FD&C Act of June 25, 1938, recognized the propriety of the Color Added process. In all such efforts Mr. Campbell had the vigorous assistance of a powerful ally, the California Citrus Growers Exchange.

If, as the result of F&DA's order of November 16th, 1955, the Color Added process was destroyed, as it would be, so that California's prior monopoly of artificial color was reinstated, the result would inevitably be chaos and ruin for the citrus industry of the United States.

Florida and Texas could not successfully market their present 30,000,000 boxes per annum of fresh fruit shipments, against California's competitive advantage of perfect artificial color. The Florida and Texas orange industry would become a canning operation, and the diversion of an additional 30,000,000 boxes into that channel would inevitably mean 50-cent oranges at the cannery platform.

The impact of the resulting tremendous volumes of cheap frozen concentrated juice on retail markets would break the price of California oranges to a point where their growers would be driven from production, and low prices for oranges at canneries would have the same effect upon Florida and Texas growers.

In short, the Color Added process is, today, one of the indispensable stabilizing factors upon which the citrus industry of the United States is dependent, not alone for continued prosperity but for its existence as an industry.

Yet F&DA would destroy that process, and seriously [fol. 47j] injure a basic agricultural industry of two States, with consequent grave consequences to the entire economy of those States, in order to enforce an arbitrary and capricious interpretation of that one word "harmless."

(3) The Evidence Upon Which the Order of the Secretary Was Entered Is Wholly Insufficient

FD&C Orange No. 2, which had been in use for some years, was re-certified under the new law in 1939.

FD&C Red No. 32 underwent exhaustive tests by eminent private toxicologists whose reports were filed with the application for certification of that color. Based thereon, temporary certification was granted by F&DA, whose toxicologists then ran certain drastic tests designed to check the private reports, and permanent certification was granted in 1939.

F&DA, however, instituted other tests that ran for five to six years (1938-1944) as a check against possible cumulative toxicity, and the results showed no such cumulative toxicity.

In late 1952, other short term tests were run for the obviously predetermined purpose of supporting the claim now made by F&DA that the color cannot be termed "harmless" because they could make test animals ill by feeding them excessive quantities of the color.

Any extended discussion of these "short-dog" 1952-53 tests is made unnecessary by the admission in the order of November 10th that the color is harmless when consumed in normal and usual amounts but there is evidence of toxicity when fed in larger amounts, i.e., an animal [fol. 47k] can be made ill if forced to consume excessive amounts.

Nevertheless we add here a short analysis of the experiments and results thereof relied upon by F&DA to support the order of the Secretary.

In Dr. Vos' testimony, shown as Exhibit No. 4 in the Hearing held January 19, 1954, a series of experimental feeding tests were reported.

On page 1, results are recorded covering an experiment conducted in 1940 in which rats were fed a daily diet containing 0.10% FD&C Red No. 32 over an extended

period of time beginning with rats which were only 21-22 days old.

On a comparable basis, assuming that a man eats an average of 4 pounds of food per day, 0.1% Red No. 32 would amount to 0.004 lbs. of color or 1.8 grams. One pound is equivalent to 453.6 grams. In order to eat 1.8 grams of color (on the basis of 0.0008 grams of color per orange) a man would have to eat 2250 oranges—peel and all—each day. This is approximately 1100 pounds of oranges that would have to be eaten per day and is approximately 7 times a man's weight.

Another comparison might be made by assuming that a man ate 6 oranges, peel and all, per day. On the basis that a color added orange contains 0.0008 grams of color, this would amount to 0.0048 grams. By comparison with the rat feeding level of 0.1% in the diet, and a man eating 4 lbs. of food per day he would have to eat 1.812 grams of [fol. 471] dye. $1.812 \div 0.0048 = 378$. Thus the rats were fed at a level of 378 times as much color as a man would get if he ate 6 oranges, peel inclusive, per day. This would amount to 1134 times as much, on the basis that a man ate two oranges per day.

On page 4 of the Exhibit is reported an experiment in which rats were fed at 2.0; 1.0; 0.5 and 0.25% levels. Since at the 0.1% level a man would have to eat 2250 oranges, then at these levels he would have to eat 45,000; 22,500; 11,250; and 5,625 oranges per day, respectively.

Assuming on the other hand that a man ate 6 oranges, peel included, per day, then on the basis of 0.0008 grams of color per orange, the total would be 0.0048 grams. On the basis of a man eating 4 lbs. of food per day, the 2.0% level would require 36.24 grams of dye. This amounts to $36.24 \div 0.0048$ or 7550. Thus the rats were fed at the rate of 7550-times as much color as a man could get if he ate 6 oranges (peel inclusive) per day. At the 0.25% level this rate is 944.

In the 1938-44 experiments reported on page 21, dogs were fed by means of capsules as much as 100 mgs. of color per kilogram of body weight per day. An average man weighs 70 kilograms (150 lbs.) and therefore would consume 7000 mgs. of color if fed at the same rate. Since a color added orange contains 0.8 mg. of color it would take 8750 oranges for a man to get 7000 mgs. of color per day. This

is approximately 4380 pounds or about 29 times as much as the man weighs.

Again assuming that a man might eat 6 oranges (4.8 mg. of color) per day then this represents that the dogs were [47m] fed at a level of $7000/4.8$ or 1458 times as great. Yet in this report in spite of the high level of feeding, it was reported that the dogs showed no ill effects except for moderate weight loss.

Subsequent to this, the same dogs were fed at the rate of 20 mg. per kilogram per day for a period of 5 years with no ill effects. This is $\frac{1}{5}$ of the 100 mg. level. On a comparable basis a man would have to eat 1750 oranges per day for the five year period. In this experiment the dogs were found to experience no ill effects.

In the 1952 experiment reported on page 29, dogs were fasted over night, then given 200 mg. of color in a capsule, and then fed two hours later. It was reported that 8 of 10 dogs developed diarrhea. This, of course, is an unnatural way of feeding. Nevertheless, on this basis a man would have to eat 7 times that amount of color, or 1400 mg. on a comparable basis and this would require 1750 oranges. This amounts to 875 pounds or more than 5 times the man's own weight. On the basis of 6 oranges per day the dogs were fed at a level of 292 times as much as a man would get if he ate 6 oranges (peel inclusive) per day.

Dr. L. G. MacDowell, Director of Research for Florida Citrus Commission, testified that his laboratory's analysis of juice extracted commercially from color-added oranges showed that it contained 0.07 parts per million of Red No. 32. It should be pointed out that rarely, if ever, does a canning plant run 100% colored oranges. Generally the fruit is a mixture of grove-run and packing house elimination. It is true also that this trace of color gets into the [47n] juice in the course of the commercial extraction and is not in the juice prior to that operation.

It may be assumed that an individual might drink as much as 8 ozs. (approximately 250 grams) of juice per day. This represents only 0.0175 mg. or 0.0000175 grams (453.6 grams per pound) of color. Assuming that a man eats 4 lbs. (1800 grams) of total food per day this amount of color is 0.000001% of the total daily diet. Compared with those

experiments in which Dr. Vos employed feeding levels of 0.1%, this represents 1/100,000 of his level or it might be said that his level was 100,000 times as much as a man might get by drinking 8 ozs. of orange juice per day.

As stated earlier, Dr. Vos reported on page 21 and 22 of Exhibit #4 that in experiments conducted in 1938-1944 dogs were fed 20 mg. of color per kilogram of body weight per day over a period of five years and no adverse effects were noted nor was there any accumulative effect.

On a comparable basis a man weighing 70 kilograms would have to eat 70×20 or 1400 mg. of dye per day. As shown above, 8 oz. of orange juice might possibly contain as much as 0.0175 mg. of dye. This then would represent $(1400 \div 0.0175)$ or about 80,000 such 8 oz. drinks or 5000 gallons of juice per day. By analogy a person could drink a 5000 gallon tank full of orange juice every day without suffering any ill effects attributable to the presence of dyestuff.

On the basis of a man drinking 8 ozs. of juice per day containing 0.0175 mg. of color, this is only 1/80,000 of the [fol. 47c] intake which caused "no effect" when the dogs were thus fed for five years.

In view of the foregoing considerations, it is submitted that the feeding levels of this dye employed in the experiments reported by Dr. Vos are fantastically greater than the amounts or levels that a person might get by eating oranges or by drinking the juice. It is clearly evident from the testimony presented at the Hearing that no evidence was submitted to show that consumption of the infinitesimal amounts of dye which might be consumed by eating color-added oranges or juice therefrom has any harmful effects whatsoever.

(4) The Order of the Secretary Is Unfounded in Law

The principal issue in these proceedings is the legality or illegality of the interpretation and construction which F&DA is attempting to place upon the word "harmless" as used in Sub-Section (b) of Section 406 of the 1938 Food, Drug and Cosmetic Act.

The order of the Secretary is based upon the theory that for a substance to be "harmless" it must have "zero

toxicity" or in other words must be completely "harmless" and utterly devoid of capability to cause any ill effect whatsoever without regard to the amount or quantity that must be ingested to cause such ill effects, which theory is contrary to law and reason and is repugnant to and violative of the fundamental rule of construction that all words and language in a statute must be given a reasonable interpretation and shall not be construed or interpreted in such manner as to produce an absurd result or defeat the plain and clear legislative intent.

In short, F&DA contends that since the word "harmless" is not modified by other language in that sub-section, it can only be construed to mean that if F&DA can make any living creature ill by feeding to that creature fantastic amounts of a certified food color, under fantastic conditions of usage, then that certified food color is not "harmless" within the meaning of the statute and may not be certified as "harmless and suitable for use" on or in foods.

The attempted construction of the word "harmless" is unlawful (and constitutes an attempt to arrogate to F&DA, by usurpation and indirection, powers which the Congress has repeatedly refused to grant to F&DA) in that:

(a) F&DA's construction of the word "harmless" is contrary to the settled rule of construction for determining the will and intent of the Congress.

(b) It is contrary to the settled rule of law that the Congress will not be presumed to have enacted or prescribed an impossible or absurd thing, i.e. (in this case) set up an impossible test as a condition precedent to an instructed action.

(c) It is contrary to the settled rule of law that the construction placed upon the language of a statute must be a "reasonable" construction.

(d) It is contrary to the settled rule of law that long [fol. 47q] continued construction of a statute by the agency charged with enforcement thereof may not be disturbed save for weighty and cogent reasons.

(e) The construction attempted by F&DA is contrary to the public interest.

These points will be discussed in that order.

(a) F&DA's construction of the word "harmless" is contrary to the settled rule of construction for determining the will and intent of the Congress.

It has long been a settled rule of construction that when the Congress uses a word or term that has theretofore been authoritatively construed, as to like use, by a Court of competent jurisdiction, it must be assumed that the Congress was familiar with such interpretation and construction and used that word or term in the same sense.

In the case of the word "harmless" as used in the Federal Food and Drug Act, the Supreme Court of the United States has construed that word to mean, in effect, that it is *harmless when consumed in the amounts and under the conditions of usual or customary usage.*

(b) It is contrary to the settled rule of law that the Congress will not be presumed to have enacted or prescribed an impossible thing, i.e., (in this case) set up an impossible test as a condition precedent to an instructed action.

F&DA's contention that the Congress prescribed "zero toxicity" when it used the word "harmless" in Sub-Section [fol. 47r] 406 (b) of the statute, does violence to the mentioned rule.

It is a well known fact of medical science that every living creature has a limit of tolerance for every substance ingested, whether that substance be an article of food, or liquid, or a food color, or a drug, or some other chemical. If *any* substance be consumed, voluntarily or involuntarily, in amounts in excess of that creature's tolerance therefor, then that creature will develop an allergy for that substance, or will otherwise be made ill by such overfeeding, even if that substance be an indispensable liquid or article of food, such as pure water or pure protein, which are the substances of life itself.

The first and usual reaction to such overfeeding of any substance is vomiting or diarrhea (suffered by dogs so overfed in F&DA tests) which are Nature's methods of ridding the body of toxic matter, or of other substances which, in themselves, are completely harmless, even bene-

ficial, but which, by such overfeeding, have become nauseating or injurious to that person or animal. Such illness, thus induced, does not even remotely imply that the substance so abused is in anywise injurious to human health when used in any imaginable amounts or under any imaginable conditions of ordinary and customary usage. F&DA are not unaware of this simple fact of medical science, hence are also advised that the results of tests employing such massive doses of these food colors are completely meaningless, insofar as concerns any possibility whatever of injury to human health.

(c) It is contrary to the settled rule of law that the [fol. 47s] construction placed upon the language of a statute must be a "reasonable" construction.

We think it is clear from the foregoing that F&DA are attempting to place upon the word "harmless" as used in Sub-Section 406(b) of this statute a construction that is not only unreasonable but is definitely repugnant to sound reason, since there is no article of food, drink, drug or color that can meet a standard of "zero toxicity" when fed in excessive amounts under abnormal conditions.

(d) It is contrary to the settled rule of law that long continued construction of a statute by the agency charged with enforcement thereof may not be disturbed save for weighty and cogent reasons.

The construction of the word "harmless" for which we contend is that construction which was administratively applied thereto in 1938 by Honorable Walter G. Campbell, Chief of the F&DA, immediately following the enactment of the 1938 FD&C Act, of which he was not only the principal author and mover for its enactment, but was also the administrative officer charged with the initial enforcement thereof.

Not until 14 years after the enactment of that Food and Drug Bill, did we hear so much as a suggestion that these colors, or any product colored therewith, could ever present any danger to human health, and we heard it then only after certain persons from the California citrus industry recommended the use of the Color Added process in that State, contrary to the wishes of the old allies of F&DA.

[47t] On this point, the United States Supreme Court has this to say:

"It is the settled rule that the practical interpretation of an ambiguous or doubtful statute that has been acted upon by officials charged with its administration will not be disturbed except for weighty reasons." (Brewster v. Gage, 280 U.S. 327.) (Emphasis ours.)

"Conceding that the proper classification of the railway is not free from difficulty, all doubt is removed by the application of the settled rule that administrative construction is entitled to great weight and should not be overturned except for cogent reasons." (U. S. v. CNS&M R.R. Co., 288 U.S. 1.) (Emphasis ours.)

As against the "settled rule" that there must be weighty and cogent reasons for upsetting the construction placed on the word "harmless" by Mr. Campbell, who wrote the Act, F&DA have advanced no reason of any kind or character for upsetting such construction except that the present Commissioner does not agree with the construction placed thereon by each of his three predecessors.

All that they can say, all that they have said, in support of the position they have taken in the instant case is that they can make a dog sick with this color if they feed enough of it to the dog, hence the color is not "harmless." They admit, as disclosed by the record, that they have not even attempted to relate the results of their alleged experimental work with any possible danger to human health; that their contention that the dye is not "harmless" is based solely [47u] upon the results of the feeding tests before mentioned. They admit that knowledge of the amount of dosage and conditions of use are necessary to a determination of toxicity or possible danger to human health, then admit, further, that they have no idea how much of this color would have to be consumed by a human being in order to adversely affect the health of that person.

(e) The construction attempted by F&DA is contrary to the public interest.

F&DA is attempting, by administrative action, to establish a new and vicious concept of law, i.e., that if any

product used as, or in, or on an article of food can, by abuse thereof, be made harmful to animal or human health, the manufacture and sale thereof in interstate commerce may be prohibited by F&DA. The food, beverage, drug and cosmetic industries would then exist only at the pleasure of whomever was appointed Commissioner of Food and Drug Administration.

Prayer for Relief

Wherefore, Petitioner hereinbefore named has caused this Petition to be signed in his behalf by his undersigned attorney and petitioner respectfully prays that this Honorable Court grant a review of the proceedings resulting in the order of the Secretary of Health, Education, and Welfare, dated November 10, 1955 as hereinbefore referred to and the order itself; that a copy of this Petition and the Petition for Stay be transmitted to the Secretary of Health, Education and Welfare of the United States; and that the Secretary be required to certify and file with this Court a transcript of the record upon which the said order was entered as required by law; and that upon [fols. 47v-51] such review the above described order be set aside insofar as it relates to FD&C Red #32 and FD&C Orange #2 and held for naught; that this Court enter an order setting aside temporarily and staying the taking effect of the order of the Secretary of Health, Education and Welfare insofar as it relates to the use of FD&C Red #32 and FD&C Orange #2 until the final determination of the petition for review in this case; that this Honorable Court enter a stay order, injunction or any and all necessary and appropriate process to postpone the effective date of the Secretary's order insofar as it relates to FD&C Red #32 and FD&C Orange #2 and to preserve status or rights of this petitioner pending conclusion of the review proceedings, or if the Court in its discretion, should determine that the relief prayed for hereinbefore should not apply to the entire order insofar as it affects FD&C Red #32 and FD&C Orange #2, then petitioner prays that the Honorable Court grant a stay order or other orders staying the operation of the Secretary's order insofar as it relates to the use of FD&C Red #32 and FD&C Orange #2 for the coloring of ma-

ture oranges, when harmless in the manner and quantity as used; and that Petitioner may have such other and further relief as the allegations herein may warrant and as to the Court may seem meet and proper.

Dated February 6, 1946

(S.) J. Lewis Hall, P. O. Box 55, Tallahassee, Florida, Attorney for Petitioner.

[fol. 52]

Saturday, December 19, 1953.

BEFORE DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Food and Drug Administration

[21 CFR Part 135]

[Docket No. FDC-60]

Color Certification

NOTICE OF HEARING TO AMEND REGULATIONS

In the matter of amending §§ 135.3 and 135.11 of the color certification regulations:

Upon the initiative of the Secretary of Health, Education, and Welfare and in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (secs. 406 (b), 504, 604, 701, 52 Stat. 1049, 1052, 1055; 21 U.S.C. 346 (b), 354, 364, 371; 67 Stat. 18), notice is hereby given that a public hearing will be held commencing at 10 o'clock in the morning of January 19, 1954, in Room G-747A, Health, Education, and Welfare Building, 330 Independence Avenue SW., Washington, D. C., for the purpose of receiving evidence upon the basis of which to amend the regulations for the certification of coal-tar colors (21 CFR Part 135, as amended 21 CFR, 1952 Supp.) in the following respects:

1. It is proposed to amend § 135.3 *List of straight colors and specifications for their certification for use in foods, drugs, and cosmetics* by deleting the names of the following straight colors and the respective specifications therefor:

FD&C Red No. 32.

FD&C Orange No. 1.

FD&C Orange No. 2.

2. It is proposed to amend § 135.11(d)(2) to read as follows:

§ 135.11 *Labeling.* * * *

(d) No batch of a mixture shall be certified under this part if:

(2) The name of such mixture is the same as or simulates the name of a previously certified batch of a mixture containing a different substance, or a different percentage of a pure dye; but this provision shall not apply if:

(i) The person who requests certification of such batch is the owner of such name and has given 3 months' written notice to the Food and Drug Administration specifying the change to be made in the composition of such mixture; or

(ii) Such change results from removal of a color from the listings in §§ 135.3, 135.4, or § 135.5.

At the hearing, evidence will be restricted to testimony and exhibits relevant and material to these proposals. The hearing will be conducted in accordance with the rules of practice provided therefor. Mr. Leonard D. Hardy is hereby designated as presiding officer to conduct the hearing in the place of the Secretary, with full authority to administer oaths and affirmations and to do all other things appropriate to the conduct of the hearing. The presiding officer is required to certify the entire record of the proceedings to the Secretary for initial decision. The proposed amendment for consideration at the hearing is subject to adoption, rejection, or modification by the Secretary as the evidence adduced at the hearing may require.

Dated: December 15, 1953.

Oveta Culp Hobby, Secretary. (Seal.)

[F. R. Doc. 53-10563; Filed, Dec. 18, 1953; 8:51 a. m.]

[fol. 53]

Thursday December 30, 1954.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[21 CFR Part 135]

[Docket No. FDC—60]

Color Certification

NOTICE OF PROPOSED RULE MAKING

In the matter of amending §§ 135.3, 135.5, and 135.11 of the color-certification regulations:

It is proposed that, by virtue of the authority vested in the Secretary of Health, Education, and Welfare by the Federal Food, Drug and Cosmetic Act (secs. 406 (b), 504, 604, 701; 52 Stat 1049, 1052, 1055; 21 U. S. C. 346 (b) 354, 364, 371; 67 Stat. 18), and upon the basis of substantial evidence received at the public hearing held pursuant to the notice published in the FEDERAL REGISTER on December 19, 1953 (18 F. R. 8600), and upon consideration of the briefs filed thereafter, the following order be made:

*Findings of fact.*¹ 1. After a hearing held beginning February 6, 1939, concerning regulations for certification of coal-tars colors, the coal-tar color now listed as FD&C Orange No. 1 (monosodium salt of 4-*p*-sulfophenylazo-1-naphthol) and the coal-tar color now listed as FD&C Orange No. 2 (1-*o*-tolylazo-2-naphthol) were found to be harmless and suitable for use in food, drugs, and cosmetics. After a hearing held beginning on July 5, 1939, concerning amendment of the coal-tar regulations, the coal-tar color now listed as FD&C Red No. 32 (1-xylylazo-2-naphthol) was found to be harmless and suitable for use in food, drugs, and cosmetics. In accordance with these findings, these three colors, among others, were listed with appropriate

¹ The citations following each finding of fact refer to the pages of the transcript of the testimony and the exhibits received in evidence at the hearing, except for citations to the FEDERAL REGISTER, where applicable.

specifications of identity and quality in the coal-tar color regulations (21 CFR 135.3) as certifiable for use in food, drugs, and cosmetics. (4 F. R. 1922, 1926, 1937, 3931, 3936, 3937; R. 46)

2. Because of advances in knowledge and techniques in the field of pharmacology, the Food and Drug Administration has initiated new tests to explore more fully the toxicity of the certifiable coal-tar colors. This involves the application of all techniques and procedures now considered necessary to assure proper evaluation. A number of these tests, with present-day techniques and procedures, have been conducted by the Division of Pharmacology of the Food and Drug Administration, using FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32.

Tests that have been terminated are:

a. FD&C-Orange No. 1:

i. Chronic feeding tests in rats with diets containing 0.1, 0.5, 1, and 2 percent.

ii. Chronic oral administration to dogs at doses of 5 milligrams per kilogram of body weight and 100 milligrams per kilogram of body weight.

iii. Cathartic tests in dogs, using single oral dose.

b. FD&C Orange No. 2:

i. Chronic feeding tests in rats with diets containing 0.01, 0.05, 0.1, 0.2, and 0.25 percent.

ii. Tests designed to determine carcinogenicity in rats, using weekly subcutaneous injections of 0.1 milliliter of a 5-percent suspension. (The test was discontinued after 8 injections, because of toxicity.)

iii. Carcinogenicity tests in mice, using subcutaneous implantation of 12.1 milligrams at intervals for 30 to 55 weeks.

iv. Chronic oral administration to dogs at doses of 5, 20, and 100 milligrams per kilogram of body weight per day.

v. Chronic feeding tests in dogs at dietary levels of 0.2 percent and 0.04 percent.

vi. Cathartic tests in dogs, using single oral dose.

c. FD&C Red No. 32:

i. Chronic feeding tests in rats, with diets containing 0.1 percent.

ii. Subacute feeding tests in rats, with diets containing 0.25, 0.5, 1, and 2 percent.

iii. Chronic feeding tests in rats, with diets containing 0.1 percent and 0.25 percent.

iv. Carcinogenicity tests in rats, using weekly subcutaneous injections of 0.1 cubic centimeter to 0.2 cubic centimeter of a 5-percent suspension. (A second experiment using weekly subcutaneous injections of 0.1 cubic centimeter of a 1-percent suspension, was discontinued after 8 injections, because of toxicity observed in rats receiving FD&C Orange No. 2 in another part of this experiment.)

v. Carcinogenicity tests in mice, using subcutaneous implantation of 10.8 milligrams at intervals for 35 weeks to 47 weeks.

vi. Chronic oral administration to dogs at doses of 5, 20, and 100 milligrams per kilogram of body weight per day.

vii. Chronic feeding tests in dogs at dietary levels of 0.04 percent and 0.2 percent.

viii. Cathartic tests in dogs, using single oral dose.

Tests that were still in progress at the time of the hearing were:

a. FD&C Orange No. 1:

i. Carcinogenicity tests in rats, using weekly subcutaneous injections of from 0.25 milliliter to 1.0 milliliter doses of a 2-percent solution.

ii. Chronic feeding tests in dogs at dietary levels of 0.2 percent and 1 percent.

b. FD&C Red No. 32:

i. Chronic feeding tests in dogs at a dietary level of 0.01 percent.

Tests of the three colors by external application to determine whether they are toxic when applied externally were being set up at the time of the hearing. (R. 8-78; Ex. 2, 3, 4)

3. The tests that have been concluded are tests normally employed to determine the toxicity of substances taken internally by man. The results of these investigations show that each of the coal-tar colors FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32, taken internally,

caused marked damage to various vital organs of the test animals, significant changes in body weight, and premature death.

FD&C Orange No. 1 caused the premature death of all rats on a diet containing 2.0 percent of the test substance. In rats on a diet containing 1.0 percent of this substance there were marked retardation of growth, increased mortality, and chronic congestion and enlargement of the spleen. These same manifestations, to a somewhat lesser extent, were encountered in rats consuming a diet containing 0.5 percent of FD&C Orange No. 1. Dogs consuming 100 milligrams per kilogram per day of FD&C Orange No. 1 died in 26 months to 33 months. They had occasional diarrhea while alive and manifested terminal weight loss. Autopsy revealed congestion and atrophy of the liver attributable to the test substance. On a diet containing 1.0 percent of FD&C Orange No. 1, dogs exhibited chronic diarrhea, rapid deterioration, and weight loss. Autopsy revealed muscular dystrophy and testicular and prostatic atrophy. These same manifestations occurred to a lesser extent in dogs on a diet containing 0.2 percent of FD&C Orange No. 1. A single dose of 100 milligrams to 200 milligrams of FD&C Orange No. 1 produced diarrhea in most dogs. Human volunteers taking 80 milligrams to 100 milligrams in a single dose experienced marked griping and diarrhea.

FD&C Orange No. 2 caused severe growth retardation and increased mortality to rats on a diet containing 0.25 percent of the test substance. At 0.2 percent of the rats' diet there were increased mortality and degeneration of the liver. At a level of 0.1 percent of the substance in the diet, the rats exhibited marked growth retardation. At a level of 0.5 percent, autopsy revealed enlargement of the right side of the heart and slight hypertrophy or hyperplasia of the cells in the liver. Five milligrams per week given to rats by subcutaneous injection caused increased mortality and moderate growth retardation. Dogs consuming 100 milligrams per kilogram of body weight per day of FD&C Orange No. 2 lost weight or gained poorly. Twenty milligrams per kilogram of body weight per day caused one dog in the experiment to gain weight poorly. Dogs on a diet containing 0.2 percent of the test substance had diarrhea at

the beginning of the experiment and exhibited rapid deterioration and weight loss. Autopsy revealed atrophy of various vital organs caused by the color. At 0.04 percent of the diet, dogs gradually deteriorated and lost weight, and autopsy revealed atrophy of various vital organs. A single dose of 200 milligrams produced diarrhea in dogs.

When FD&C Red. No. 32 was fed to rats at a level of 2.0 percent of the diet, all the rats died within a week. At a 1.0-percent level, death occurred within 12 days. At 0.5 percent most of the rats died within 26 days. At 0.25 percent approximately half of the rats died within 3 months. All the rats showed marked growth retardation and anemia. Autopsy revealed moderate to marked liver damage. Sim- [fols. 54-56] ilar but less severe results were obtained with rats on a diet containing 0.1 percent of FD&C Red No. 32. In addition to liver damage, however, autopsy also revealed enlargement of the right side of the heart in this latter group. Subcutaneous injection of approximately 10 milligrams per week caused death within 8 weeks to most rats on the experiment. These rats exhibited anemia, hemorrhage, and reduction in the size of the liver. Dogs taking 100 milligrams per kilogram of body weight per day showed moderate weight loss. A level of 0.2 percent of FD&C Red No. 32 in the diet of dogs caused rapid deterioration and weight loss and sporadic diarrhea; 0.04 percent caused gradual deterioration and weight loss, sporadic diarrhea, moderate atrophy of vital organs, and muscular dystrophy; 0.01 percent in the diet caused weight loss and the death of one out of four dogs. A single oral dose of 100 milligrams or 200 milligrams gave diarrhea in the majority of the dogs tested.

The results of pharmacological tests, conducted by qualified investigators using recognized scientific methods, establish that the colors are not harmless substances, but on the contrary are definitely toxic and exert pronounced physiological effects on body tissue. The experimental work on man is limited, and except for Orange 1, adverse effects on man have not been definitely confirmed. (R. 8-87, Ex. 2, 3, 4)

4. The coal-tar colors listed in the regulations as FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32 may be used at present in externally applied drugs and cosmetics as well as products for internal consumption. Tests

designed to examine the toxicity of these colors, when used externally, are not complete. (R. 46-48, 63-65)

5. Modification of 21 CFR 135.11(d)(2) to eliminate the requirement for 3 months' written notice of change in composition of a coal-tar color mixture will facilitate the marketing of substitute mixtures and reduce confusion that may result from the deletion of a straight color from the listings at 21 CFR 135.3, 135.4, and 135.5. (R. 88, 89)

Conclusions. 1. Based upon the evidence of toxicity presented at the hearing, the coal-tar colors FD&C Orange No. 1 (monosodium salt of 4-*p*-sulfophenylazo-1-naphthol), FD&C Orange No. 2 (1-*o*-tolylazo-2-naphthol), and FD&C Red No. 32 (1-xylylazo-2-naphthol), described in the coal-tar color regulations, 21 CFR 135.3, are not harmless and suitable for use within the meaning of sections 406(b), 504, and 604 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346(b), 354, and 364) in coloring food or for use in coloring drugs or cosmetics intended for other than external application.

2. The coal-tar colors FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32 should be deleted from the listing at 21 CFR 135.3, since the Secretary cannot continue to list these colors as colors that the Food and Drug Administration will certify as harmless and suitable for use in coloring food or in coloring drugs and cosmetics intended for other than external application.

3. Colors conforming to the present regulations and specifications for FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32 should be added to the listing at 21 CFR 135.5, for use in coloring externally applied drugs and cosmetics only.

4. The provisions of 21 CFR 135.11(d)(2) requiring 3 months' written notice of a change in the composition of a coal-tar color mixture should be waived when such change is made necessary by deletion of one or more straight colors from the listing at 21 CFR 135.3, 135.4, or 135.5.

Therefore, it is proposed that Part 135—Color Certification be amended in the following respects:

1. In § 135.3 (a), delete the colors FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32.

2. Add the following to § 135.5 (a):

EXT D&C ORANGE No. 3

Specifications

Monosodium salt of 4-*p*-sulfophenylazo-1-naphthol.

Volatile matter (at 135° C.), not more than 10.0 percent.

Water-insoluble matter, not more than 0.3 percent.

Ether extracts, not more than 0.2 percent.

α-Naphthol, not more than 0.1 percent.

Chlorides and sulfates of sodium, not more than 4.0 percent.

Mixed oxides, not more than 1.0 percent.

Orange II, not more than 5.0 percent.

Pure dye (as determined by titration with titanium trichloride), not less than 85.0 percent.

EXT D&C ORANGE No. 4

Specifications

1-*o*-Tolylazo-2-naphthol.

Volatile matter (at 100° C.), not more than 0.5 percent.

Sulfated ash, not more than 0.3 percent.

Water-soluble matter, not more than 0.3 percent.

Matter insoluble in carbon tetrachloride, not more than 0.5 percent.

o-Toluidine, not more than 0.05 percent.

β-Naphthol, not more than 0.05 percent.

Pure dye (as determined by titration with titanium trichloride), not less than 98.0 percent.

Melting point, not less than 128.0° C.

EXT D&C RED No. 14

Specifications

1-Xylylazo-2-naphthol.

Volatile matter (at 100° C.), not more than 0.5 percent.

Sulfated ash, not more than 0.3 percent.

Water-soluble matter, not more than 0.3 percent.

Matter insoluble in carbon tetrachloride, not more than 0.5 percent.

Xylidene, not more than 0.1 percent.

β-Naphthol, not more than 0.05 percent.

m-Xylidine in xylidine obtained by reduction of the dye, not more than 30.0 percent.

Pure dye (as determined by titration with titanium trichloride), not less than 97.0 percent.

Boiling range of xylidine, obtained by reduction of the dye, 95 percent between 212°-232° C.

3. Amend § 135.11(d)(2) so that, as amended, it will read as follows:

§ 135.11 *Labeling.* . . .

(d) . . .

(2) The name of such mixture is the same as or simulates the name of a previously certified batch of a mixture containing a different substance, or a different percentage of a pure dye; but this provision shall not apply if:

(i) The person who requests certification of such batch is the owner of such name and has given 3 months' written notice to the Food and Drug Administration specifying the change to be made in the composition of such mixture; or

(ii) Such change results from removal of a color from the listings in §§ 135.3, 135.4, and 135.5.

Any interested person whose appearance was filed at the hearing may, within 30 days from the date of the publication of this tentative order in the **FEDERAL REGISTER**, file with the Hearing Clerk, Department of Health, Education, and Welfare, Room 5440, Health, Education, and Welfare Building, 330 Independence Avenue SW., Washington, D. C., written exceptions thereto. Exceptions shall point out with particularity the alleged errors in this tentative order and shall contain specific references to the pages of the transcript of the testimony or to the exhibits on which such exceptions are based. Such exceptions may be accompanied by a memorandum or brief in support thereof. Exceptions and accompanying memoranda or briefs shall be submitted in quintuplicate.

Dated: December 22, 1954.

Nelson A. Rockefeller, Acting Secretary. (Seal.)

[F. R. Doc. 54-10346; Filed, Dec. 29, 1954; 8:49 a. m.]

[fol. 57] Before the Secretary of Health, Education, and Welfare.

In the Matter of: Amending Sections 135.3 and 135.11 of the Color Certification Regulations of the Department of Health, Education, and Welfare.

(21 CFR, Part 135)

(Docket No. FDC-60)

Brief of Chase & Company and Randall Chase.

STATEMENT

On January 19, 1954, pursuant to notice of hearing of [fol. 58] proposed rule making, a hearing was held before Leonard D. Hardy, Presiding Officer, acting on behalf of the Secretary of Health, Education, and Welfare. The hearing dealt, in part, with the proposal of the Secretary to amend Section 135.3 of the color certification regulations by deleting the names of FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32 and the respective specifications therefor. Chase & Company which raises oranges in the State of Florida and ships them in interstate commerce, entered an appearance and participated in the hearing.

The primary purpose of the hearing was receive evidence for the purpose of determining whether to amend the regulations for the certification of coal-tar colors by deleting from Section 135.3 the dyes specified above because of data which had been obtained by the Food and Drug Administration indicating that the substances were not harmless, as required by Section 406(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 346(b). On December 22, 1954, a notice of proposed rule making was issued by the Acting Secretary. Based upon the findings of fact set forth in the notice, the Acting Secretary concluded in part that the three dyes are not harmless and suitable for use in coloring food and may not continue to be listed and certified for that purpose.

The notice of proposed rule making states that any interested person whose appearance was noted at the hearing may file written exceptions to the tentative order. Chase

& Company, and Randall Chase, on behalf of the company and on his own behalf as a consumer, believe that an extremely important problem is presented from the viewpoint [fol. 59] of those growers of oranges who do not wish to perpetrate a fraud upon the consumer, and that the problem directly concerns the public health and purse. In view of these considerations, we seek here to establish:

(1) The findings and conclusions of the Acting Secretary that the colors involved are not harmless are supported by Substantial and uncontradicted evidence in the record.

Allowed.

(2) The findings and proposed order are defective in not dealing with the problem of whether the dyes, particularly when employed on oranges, do not render the food adulterated and misbranded under the Federal Food, Drug, and Cosmetic Act and thus can be said to be "suitable for use" under Section 406(b) of the statute.

Denied.

(3) Exception is and must be taken to those portions of the order, "2" and "3" of the proposed amendments to Part 135—Color Certification, purporting to permit various colors to be utilized in foods, since no finding has been made that the dyes, when used in or on food, do not adulterate or misbrand the food in violation of the Act and thus can be said to be "suitable for use."

Denied.

[fol. 60]

Argument

I

The proposed order and findings of fact with respect to "harmlessness" are based on, and supported by, substantial evidence of record at the hearing.

By reason of advances in the vital field of pharmacology and the results of experimental work in this country and other countries which created serious doubts as to the chronic toxicity and carcinogenicity of the certified coal-tar colors, the Food and Drug Administration initiated labo-

ratory and experimental work to evaluate the long-range hazards created by the use of these dyes. It may be added, parenthetically, that such a burden was not intended to be placed, and should not have been placed, upon the Food and Drug Administration, with its extremely limited appropriations. The reasons which commendably caused the Administration to conduct the essential research should certainly have impelled those who manufacture and utilize the colors to perform the necessary tests to determine whether a hazard to the public health exists. The burden of establishing that a synthetic dye is both harmless and suitable for use is on them.

The only pharmacological evidence bearing on the question whether the colors here involved can be said to meet the standard of harmlessness was that presented by Dr. Bert J. Vos, Assistant Chief of the Division of Pharmacology of the Food and Drug Administration. There is no need to dwell in this brief upon his testimony, which was not contradicted in any respect. His testimony, and the [fol. 61] data which he submitted, disclose that all three dyes possess a degree of toxicity which removes them from the category of "harmless."

The findings set forth the results of the laboratory work performed by the Food and Drug Administration, and reveal beyond any doubt that the colors cannot be said not to present a hazard. Our brief submitted at the conclusion of the hearing, to which we refer and request that it be considered in this connection as constituting part of this brief, makes detailed references to the evidence of record amply supporting the findings of the Acting Secretary. Finding of Fact 3, predicated upon the uncontradicted evidence of record, indicates quite glaringly the adverse physiological consequences of the ingestion of the colors by test animals. The evidence entirely supports the finding that the colors are not harmless but on the contrary are definitely toxic and exert pronounced physiological effects on body tissue. It appears to us that one must possess a high degree of temerity to urge, after a consideration of these findings, that these dyes should nevertheless be employed in or on any foods in amounts smaller than those fed to the laboratory animals. The more pertinent question is why

these colors, performing not the slightest service to the consumer, were continued in use by their manufacturers although doubt as to their toxicity and carcinogenicity has existed for some time.

Particularly is this true in view of the fact that carcinogenicity tests have not been completed. Certainly the Secretary cannot shut her eyes to what is scientifically accepted, and that is that coal-tar colors are suspect with respect to their effect in causing cancer, that a cancer [fol. 62] produced by a substance such as a coal-tar dye may not reveal itself for many years and may be caused by minute amounts, and that no comprehensive work has been performed to determine even with a reasonable degree of certainty whether the three coal-tar colors here involved are or are not carcinogenic. It is true that these colors were once approved and that the burden of going forward with evidence pertaining to harmlessness may be on the Government. But the burden of proof never changes—under Section 406(b) the burden is on those who wish to market a coal-tar color to establish that it presents no hazard, and particularly from the viewpoint of carcinogenicity. The failure to perform any work of this vital character or to present an iota of evidence at the hearing tending to establish the freedom of the colors from cancer producing consequences or other hazard would of itself be sufficient to demonstrate that the dyes have not been shown to be harmless. The Secretary may certainly take notice of a plethora of scientific testimony bearing on this cancer problem. One example is that given by Dr. Francis E. Ray, Director, Cancer Research Laboratory, University of Florida, at the Hearings held before the House of Representatives Committee to Investigate the Use of Chemicals in Food Products, Eighty-First Congress, Second Session. This is what Dr. Ray said, in part, at page 641, on the over-all problem of the possible cancer-producing quality of the synthetic coal-tar dyes:

“A whole series of the class known as AZO Compounds related to the dye, butter yellow, have been found to produce cancer. According to the twenty-sixth annual report of the British Empire Cancer Campaign (p. 198) two food dyes in general use containing the AZO group [fol. 63] were examined. One of these, oil orange E,

caused tumors in 7 out of 17 mice, 14 months after the start of the experiment—14 months is about half the life of a healthy mouse. An eighth mouse showed extensive liver damage.

"I would suggest to the committee that we have not adequately tested our so-called certified pure-food colors for carcinogenic properties. These substances should be tested by feeding, painting, and injection for a period of at least 18 months. Each animal should be examined both grossly and microscopically by a competent pathologist."

We contend that it is somewhat disingenuous under these circumstances, to state that "There is, however, no evidence that, in the amounts used, and in the manner of use, in the coloring of citrus fruit, the product so colored is not safe for human consumption".¹ We urge that any statement, particularly if it emanates from the Government, whereby an impression is created that the colors or foods containing them are safe, is an unintended disservice to the public. True, the evidence does not establish beyond any doubt that these dyes have been shown to have caused injury to man. But as Finding of Fact 3 itself points out, the most that can be said in this connection is that:

"The experimental work on man is limited, and except for Orange 1, adverse effects on man *have not been definitely confirmed*" (Italics supplied.)

[fol. 64] And if anything is well-settled in food and drugs law, it is that Sections 403(a) and 201(n) of the Act prohibit statements which are misleading even though not literally false. See *United States v. 95 Barrels of Vinegar*, 265 U.S. 438, 442-443. The very purpose of Section 201(n) of the Act is to prohibit deceptions of this character, and a statement that the colors have not been demonstrated to be harmful to humans in the amounts utilized, without coupling it with a statement of the fact that the colors are poisonous or deleterious (and therefore not harmless) substances is at best deceptive and a

¹ See letter dated February 7, 1955, from the Commissioner of Food and Drugs to Senators Holland and Smathers.

failure to reveal a material fact. The misleading impression created by the sentence quoted above (which can with such facility be taken out of context) is not appreciably weakened by preceding the sentence with a statement that "Recent investigations show that these colors, when fed in substantial amounts, show evidence of toxicity." We urge most seriously, therefore, that steps be taken to dispell such misleading impression—otherwise the high standard of truth called for by the Act has not been met. See, for example, *United States v. 12 Bottles of Esterex* (E.D. Mo., 1946), *Kleinfeld and Dunn, "Federal Food, and Cosmetic Act, 1938-1949"*, p. 523. In that case, a solution of monochloroacetic acid, which the Government regarded as a poisonous or deleterious substance, was shipped in interstate commerce. Its labeling did not contain any false statement, but it was the Government's position, under Sections 403(a) and 201(n) of the statute, that the labeling was misleading in that it failed to reveal the fact that the article contained a poisonous substance, and that such a fact was material in the light of the representation that the article was to be employed as a [fol. 65] component of food. In accepting the Government's position and condemning the product, the Court found, in part:

"There is nothing on the label to indicate that monochloroacetic acid is poisonous, and the label does not sufficiently caution the careless, the unthinking or the ignorant of the fact that the said article contains a poisonous, toxic and caustic substance. . . ."

"Although there is no statement on the label which is untrue, the label is misleading in that it fails to reveal that the said article contains a poisonous, toxic and caustic substance and such fact is material in the light of the representations that said article is to be used as a component of liquids for human consumption."

On the basis of the Government's own experimental work, it cannot be said, without creating a misleading impression, that there is no evidence that oranges containing the dyes are not safe for consumption. Can it be said, rather, that citrus fruit containing the dyes are safe for human consumption? The only statement which would be fair to the public, both here and abroad, would be one which

would say in substance: "The coal-tar colors are poisonous substances and therefore cannot be said to be harmless. We are suspicious, but so far it has not been established beyond doubt that these dyes, in the amounts used in foods, including oranges, have caused injury to humans. We cannot say that they have not caused damage, and we are continuing our experimental work." Particularly should this be true in view of the fact that the present proceedings have been brought to decertify colors which have been [fol. 66] widely used for many years with Governmental clearance and approval notwithstanding that they are not harmless substances.

II

The criterion of Section 406(b) is whether a coal-tar dye is a harmless substance, and not whether the amount added to a food results in the food being rendered harmful to health.

"In connection with the interpretation of a law such as the Federal Food, Drug, and Cosmetic Act, designed to protect the public health, there is no reason for an unnecessary limitation of the protection afforded to the consumer by the plain language of the statute. *United States v. Dotterweich*, 320, U.S. 277. Section 406(b) of the Act provides, in explicit language, that "The Secretary shall promulgate regulations providing for the listing of coal-tar colors which are harmless * * *." If Congress had intended to say that the Secretary shall promulgate regulations providing for the listing of coal-tar colors "which, in the amount used in a food, are harmless for use in such food", or "which, in the amount used in a food, do not render the food harmful", Congress would have said so, the words were readily available.

It is apparent, from both the specific language of subsection (a) of Section 406 and the pertinent legislative history, that the Congressional design was to exclude from the Nation's food supply poisonous and deleterious substances in any amount whatever unless they are required in or can not be avoided by good manufacturing practice, and to establish tolerances for such poisonous or deleterious [fol. 67] substances when they are so required or can not be so avoided. Subsection (b), which is in *pari materia*

with subsection (a), similarly prohibits the employment in food of any coal-tar color which cannot be demonstrated to be a harmless substance. The only distinction between the two subsections is that Congress chose not to permit the establishment of any tolerances for harmful coal-tar colors such as are here involved, apparently because there was no proof whatever that dangerous coal-tar dyes are required in the production of any food or cannot be avoided by good manufacturing practice.

In our brief submitted after the conclusion of the hearing, we adverted at considerable length to the legislative history of the Act, which reveals beyond any doubt the design of Congress to prohibit entirely those coal-tar colors which cannot be considered, regardless of amounts employed, to be harmless substances, and not proscribe merely the employment of such quantities as might render the particular food containing the color harmful to health. We also discussed the unvarying administrative position of the Food and Drug Administration, and the judicial holdings, which are in complete accord with the language and legislative history of the Act. We respectfully refer to our prior brief as if the applicable portions, in this connection, were set forth here in full.

Philosophy of the Act

The entire philosophy of the Federal Food, Drug, and Cosmetic Act envisages the proscription from the dietary of the Nation of all amounts of substances which are or [fol. 68] may be harmful, with the specific, limited exception contained in Section 406(a). For example, in Statement of General Policy or Interpretation, Section 3.14, dated January 13, 1950 (Kleinfeld and Dunn, "Federal Food, Drug and Cosmetic Act, 1949-1950," p. 285), the Federal Security Administrator announced that he regarded dulcin and P-400, artificial sweeteners, as poisonous substances which had no place in any food. This position was taken in view of the effect of the ingestion of the substances by rats, notwithstanding that it had not been established that the ingredients produced toxic effects in humans in the amounts customarily employed in foods.

The same problem was recently highlighted in connection with coumarin, which had been used for many years

as a food flavor without any indication that it was injurious. After a public hearing which revealed that coumarin had produced toxic results in test animals, the Department of Health, Education, and Welfare removed the substance as an optional ingredient for use in cacao products, notwithstanding that there was no evidence that, in the amounts in which it was employed in food, it produced any adverse physiological effects in humans.

There would seem to be no need for laboring the point unduly. It is apparent that Congress deliberately provided against the utilization of any amount whatever of a coal-tar dye which, standing by itself, cannot be said to be harmless. The reason for this, and for the similar result which follows where Sections 401 and 406(a) are involved, are obvious. Substances which are or may be dangerous should [fol. 69] not be inflicted upon the consuming public in any amounts. Even if it is probable that a small amount of a poisonous or harmful substance such as the coal-tar dyes may not cause harm in a comparatively short period of time, there is no assurance that its ingestion over long periods of time, and the consumption of small amounts of other and diverse poisonous, dangerous, or harmful substances, will not cause carcinogenic or other adverse physiological effects. The soundness of and necessity for this approach were set forth most eloquently in December of 1952 by the United States Court of Appeals for the Third Circuit in *Atlas Powder Company v. Ewing*, 201 F. 2d 347. In that case, the petitioners sought review of an order establishing a definition and standard of identity for bread which did not permit the use of petitioners' chemical softeners. There was no proof that, in the amounts in which the softeners were employed in bread, harm resulted to humans. Nevertheless, the Federal Security Administrator concluded that the softeners could not be used in bread because the results of their ingestion by test animals revealed that the safety of the substances had not been established. As stated, the Administrator could not determine (as the Secretary cannot determine with respect to the use of coal-tar colors on oranges) that, in the amounts utilized in bread, the softeners were deleterious to the health of humans. In affirming the decision of the Administrator, however, the Court set forth the rationale which is a fortiori applicable to coal-tar colors:

"One making a rule for the future which in practical effect will determine whether millions of people shall eat something every day may reasonably refuse to subject [fol. 70] the general public to even slight risks and small deceptions. In these circumstances, the fact that administrative action has been dominated by great caution but serves to emphasize the reasonableness of the Administrator's conduct."

Use of the Colors in Oranges

It is well-known that orange juice from Florida oranges is consumed practically every day by large numbers of persons in this country, that marmalades frequently contain orange rind, that candied orange peel is consumed, and that in baking cake some women grate the rind to obtain additional flavor.

Mr. Louis C. MacDowell, Research Director of the Florida Citrus Commission, testified (R. 101, 102) with respect to the quantities of coal-tar dyes found in whole fruit, orange peel, candied orange peel, orange marmalade and orange juice. The amount of coal-tar dye found ranged from 17.63 to 24.39 parts per million in the peel of fresh fruit, to .04% to .07% parts per million in orange juice. There is not the slightest basis for any contention that those amounts may be ignored, for we have shown that a coal-tar color which has not been shown to be a harmless substance may not be employed in or on foods in any amount.

Certainly this would seem to be particularly true with regard to oranges, which in one form or another are consumed every day in the year "by the strong and the weak, the old and the young, the well and the sick". (See *United States v. Lexington Mill and Elevator Co.*, 232 U.S. 299). As we have demonstrated, Congress did not provide, in [fol. 71] Section 406(b), for the taking of any chances with the health of the inhabitants of this country. None should be taken with a synthetic dye, for example, which from a chronic viewpoint has greater toxicity in rats than carbolic acid and whose freedom from hazard, including carcinogenicity, has not been established. Even if there were any provision in subsection (b) for the making of exceptions, and the subsection contains none, the exception should not be made in connection with the use of the three coal-tar dyes

here involved on oranges, consumed by all segments of the population, and in all degrees of health. This is particularly true since there is not an iota of evidence that the dyes serve any useful purpose whatever or that their addition to oranges does not defraud the consumer, conceal inferiority, or make the product appear better and of greater value than it actually is.

III

A coal-tar color may not be listed as "suitable for use" under Section 406(b) if it violates other provisions of the Act.

Section 406(b) provides that the Secretary shall promulgate regulations providing for the listing of coal-tar colors which not only are "harmless", but also are "suitable for use", in food. Regardless of the question of toxicity, we cannot comprehend how, under a remedial statute such as the Federal Food, Drug, and Cosmetic Act, clearly designed to protect the consumer, it can be maintained that a coal-tar dye can be said to be suitable for use on oranges unless it is demonstrated that the consumer is not being [fol. 72] deceived and that the Act is not otherwise violated. We urge that evidence with respect to any coal-tar color used or proposed for use in foods must be presented to the Secretary, and findings made by her, as to whether the dyes do or do not conceal inferiority, do or do not make the food appear better or of greater value than it is, and do or do not constitute a fraud upon the consuming public. Only upon the basis of such evidence, as well as upon evidence of harmlessness, can the Secretary comply with the Congressional directive, in Section 406(b), that in order for coal-tar colors to be listed they must be harmless and suitable for use.

By letter dated October 13, 1952, addressed to Mr. Randall Chase, the Associate Commissioner of Food and Drugs stated in part:

"Let me say at the outset that this Administration is in agreement with your conclusion that the use of added color on oranges is inherently deceptive and is contrary to the interests of both consumers and producers."

We are in entire accord with that administrative position. We are in disagreement, however, with the view apparently

taken at that time that the legislative history of the Act requires a conclusion that the law does not ban the use on oranges of such dyes as create an economic cheat upon the consumer. We believe it would take specific language indeed to indicate a Congressional intent to permit the use on oranges of any coal-tar color which "is inherently deceptive and is contrary to the interests of both consumers and producers." We are not contending that [fol. 73] no coal-tar dye may be used under any circumstances, for Section 402(c) does make a reference to the employment of color on oranges. But nothing in the Section, or in the legislative history reveals a design to permit the use of those dyes which clearly violate the explicit provisions of the statute dealing with the adulteration and misbranding of food products. Contrariwise, as we shall demonstrate, what there is in the legislative history leads to the opposite conclusion.

1

A separate finding must be made with respect to whether a coal-tar dye is "suitable for use."

No citation of authorities is needed to support the virtually universal maxim of statutory construction that words are not inserted in a law for no purpose. The term "suitable for use" cannot refer to the harmlessness of a coal-tar dye, for such a construction would add nothing to the word "harmless" and render "suitable for use" superfluous. The phrase, therefore, must refer to something other than hazard to health. Again, considering the remedial purposes of the Act, stressed again and again by the executive branch, as well as by the judicial and legislative branches, of our Government, "suitable for use" must be construed to refer to economic protection of the consumer.

Under Section 406(b), "suitable for use" is as much a prerequisite to approving a coal-tar color as is "harmless". Findings dealing with both aspects must, therefore, be made by the Secretary—otherwise the statutory mandate [fol. 74] is not observed and the judicial review provided by the Act cannot be obtained. As stated in *Twin City Milk Producers Association v. McNutt*, 122 F. 2d 564 (C.A. 8), "But where a Court is charged with the duty of reviewing the validity of an administrative agency's order, it has, up to the present time at least, refused the stamp of judi-

cial approval, unless the order affirmatively demonstrated a compliance with all express and implied conditions underlying the exercise of the power." See, also, *A. E. Staley Manufacturing Co. v. Secretary of Agriculture*, 120 F. 2d 258 (C.A. 7).

2

The Act does not authorize the listing of a coal-tar color whose use will violate specific statutory provisions.

As we have pointed out, there is no indication that, by utilizing the language found in Section 402(c), Congress intended to extend a blanket authorization to orange growers to conceal the inferiority of their product, deceive the consumer, and make their product better and of greater value than it is.

There is nothing persuasive in the legislative history of the Act which reveals any design to permit a defrauding of the consumer. As a matter of fact, at one step of the progress in Congress of the various bills which culminated in the passage of the statute, a specific attempt was made to authorize the coloring of oranges notwithstanding the adulteration and misbranding provisions of the law. When S. 2800, 73d Congress, was reported out by the Senate Committee on Commerce, the following paragraph was added:

[fol. 75] "Nothing in this Act shall be construed to prohibit the enhancement of the color of mature and whole: some citrus fruits to the varietal color thereof, by means harmless to the consumer of such fruits, nor to require any declaration of such enhancement, by labeling or otherwise." (Dunn, "Federal Food, Drug, and Cosmetic Act," p. 94.)

A subsequent reprint of the bill with Committee Amendments contained the same provision. (Dunn, *supra*, p. 169.)

It will be seen, therefore, that Congress gave definite thought to permitting the use of coal-tar dyes on oranges notwithstanding the resulting economic cheat of consumers. In fact, Congress even gave consideration to not requiring that the addition of the color be declared on the labeling of the food containing it. If the language quoted above had been retained, it might be argued that any coloring, even if a food containing it would otherwise have been

misbranded under Section 403(a), and adulterated under Section 402(b), could be utilized. Nor would Section 403(k), requiring a declaration of the presence of artificial coloring, have been applicable. But Congress chose not to include the quoted provision, not to permit the use of those colors which would act as a fraud upon the public; just as Congress determined to retain the applicability of Section 403(k). The legislative history, therefore, requires the construction that coal-tar dyes which are harmless may be employed, but only if they do not contravene any other provisions of the Act. The burden of establishing that the relevant statutory provisions will not be violated, that the consumer will not be defrauded, has not been [fol. 76] met in the slightest respect by those who seek to employ coal-tar colors on oranges. It is well-settled that economic adulteration cannot be cured by any form of labeling. *United States v. 2 Bags * * * Poppy Seeds*, 147 F. 2d 123 (C.A. 6); *United States v. 36 Drums "Pop'n Oil"*, 164 F. 2d 250 (C.A. 5). Since the Government has recognized that the use of the colors on oranges is "inherently deceptive", no labeling can be legal. Assuming for the sake of argument, however, that some form of truthful labeling would be permitted (although none should be), Sections 403(a) and 201(n) would require a declaration that the dye had been added to conceal inferiority.

3

Section 403(k) does not authorize the introduction into interstate commerce of a citrus fruit containing a dye which conceals the inferiority of the fruit and makes it appear better and of greater value than it is.

The heating and dyeing of an orange with a coal-tar color is a chemical process designed to imitate natural maturity. Its purpose is to conceal immature skin and other inferiority, to disguise blemishes, and to add a deeper color to the naturally pale color of the orange for the purpose of causing the consumer to think he is getting a naturally tree-ripened fruit. To a very considerable extent, the consumer makes purchases on the basis of the color and external appearance of the orange, and color is one of the considerations in grading the fruit. As indicated above in this brief, the economic cheat caused by adding a dye to oranges has been recognized by the Food and Drug

Administration. Certainly the use of these colors does not [fol. 77] add any food value to the fruit or benefit the consumer in the slightest respect.

The legislative history of the Federal Food, Drug, and Cosmetic Act discloses that, in inserting Section 403(k), which permits the addition of artificial coloring if the food containing it bears labeling stating that fact, it was the Congressional intent to ban the transportation in interstate commerce of products which had been adulterated by the addition of artificial coloring. The predecessor of Section 403(k) appeared in S. 5, 74th Cong., 1st Sess. As reported by the Committee on Commerce, Section 302(k) of the bill (which later became in substance Section 403(k)), declared a food to be misbranded—

“If it bears or contains any artificial flavor, artificial color, or chemical preservative, and it fails to bear a label stating that fact.”

The Committee report on the bill said of this provision: “Paragraph (k) is intended to insure label declaration of additions of artificial color, artificial flavor, or chemical preservatives. This paragraph does not exempt products subject to it from the other provisions of the bill. *If artificial color is harmful or creates a deceptive appearance, the product will be subject to the applicable provisions of Section 301 [the adulteration section which included the counterpart of Section 402(b)(3) and (4)]*” (Italics supplied) (S. Rep. No. 361, 74th Cong., 1st Sess., p. 13.) [fol. 78] Before the bill passed the Senate, Section 302(k) was amended to read:

“If it bears or contains any artificial flavor, artificial color, or chemical preservative, which is not prohibited by section 301, and it fails to bear a label stating that fact.”

Section 301 defined a food as adulterated—

“ . . . (3) If damage or inferiority has been concealed in any manner; or (4) if any substance has been added thereto or mixed or packed therewith so as to increase its bulk or weight, or reduce its quality or strength, or create a deceptive appearance.”

When this bill was reported by the House Committee, the words “which is not prohibited by section 301” were deleted. The Committee’s explanation was as follows:

“Section 302(k): In this paragraph the words ‘which is not prohibited by section 301’ were omitted as being sur-

plusage, and furthermore their presence created confusion as to the meaning of the words 'stating that fact' which appear later in the paragraph (H. Rep. No. 2755, 74th Cong., 2d Sess., p. 5.)"

Implicit in the explanation of the House Committee is its agreement with the expression of legislative design in the excerpt from the Senate Report.

It is entirely clear, therefore, that the Congressional intent in enacting Section 402(b) and Section 403(k) was to prescribe two separate prohibitions, each essentially different from the other. The authority in Section 304(k) to use artificial coloring, artificial flavoring, and chemical preservatives is limited to those products whose inferiority is not concealed, and which are not made to appear better or of greater value than they are, by the addition of an artificial ingredient. This legislative motivation is consonant with the objects of the Act "to prevent the misuse of the facilities of interstate commerce in conveying to and placing before the consumer misbranded and adulterated articles * * *". *McDermott v. Wisconsin*, 228 U.S. 115, 131. This construction of Sections 402(b) and 403(k) has been invariably urged by the Food and Drug Administration, and the Courts have accepted this interpretation. See, for example, *United States v. Two Bags * * * Poppy Seeds*, 147 F. 2d 123 (C.A. 6), where the Court sustained the Government's contention that the addition of charcoal pigment to white poppy seeds so that they resembled more expensive seeds, the product then being shipped to jobbers truthfully labeled under Sections 403(a) and 403(k), concealed inferiority and made the product appear better or of greater value than it was, in violation of Section 402(b).

4

Under Section 406(b), no distinction can be made between oranges and other foods.

We have pointed out that Section 406(b) proscribes any amount of a substance which has not been demonstrated to be a harmless, non-poisonous substance, even if it has not been established that the amount contained in a particular food will cause harm to humans. The amount of the coal- [fol. 80] tar dyes found in the juice of oranges and in the peel does not alter this concept in any respect, particularly

since, as we have stated, orange juice is consumed every day by all segments of the population, including babies, children, the aged and infirm. If the colors were permitted on oranges, although there could not be the slightest legal justification for such authorization, the provisions of Sections 403(a) and 201(n), as construed by the Food and Drug Administration and interpreted by the Courts, would require that the consuming public be informed not only of the material fact that the dye conceals inferiority, but also of the material fact that the color is a poisonous substance. See *United States v. 12 Bottles of Esterex*, supra. The orange would be compelled to declare "Artificial coal-tar color, a poisonous substance, added to conceal inferiority." In this connection, we believe we should direct attention to the fact that the term "color added", as presently employed on oranges to which a coal-tar dye has been added, cannot be said to comply with the provisions of Section 403(k). The Section does not state that:

"A food shall be deemed to be misbranded—If it bears or contains any flavoring, coloring, or preservative, unless it bears labeling stating that fact * * *." Rather, the section is specifically directed at the addition of artificial or synthetic substances; thus it provides quite clearly that:

"A food shall be deemed to be misbranded—If it bears or contains any *artificial* flavoring, *artificial* coloring, or chemical preservative, unless it bears labeling stating that fact * * *." (Italics supplied.)

[fol. 81] It is apparent, therefore, that Section 403(k) requires labeling which informs the consumer that an artificial color has been added, that the phrase "stating that fact" refers to the fact that an artificial substance has been employed, and that it is violative of the Act and a disservice to the consuming public to permit the use of wording such as is currently found on oranges containing a synthetic coal-tar dye.²

² See S. Rep. No. 361, 74th Cong., 1st Sess.: Paragraph (k) is intended to insure label declaration of additions of artificial color, artificial flavor, or chemical preservatives." (Dunn, supra, p. 248.) See also S. Rep. No. 91, 75th Cong., 1st Sess.:

"Requires label declaration of artificial colors and artificial flavors in food." (Dunn, p. 680.)

Conclusion

The record of the hearing fully supports the findings that FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32 are not substances which have been shown to be harmless for use in or on any food, including oranges. Consequently, for this reason alone, colors may not be permitted use in the dietary of the Nation and Section 135.3 of the color certification regulations should be amended, as set forth in the proposed order, by deleting the names of the three dyes and the respective specifications therefor.

The findings and order should make a determination, in addition, with respect to whether the colors involved and any other colors referred to are suitable for use in that they do not conceal inferiority, or make a food appear better or of greater value than it is, or otherwise deceive the consumer, in violation of Section 402(b). No label [fol. 82] declaration can cure such economic adulteration, but any statement purporting to comply with the provisions of Sections 403(a) and 201(n), as well as with 403(k), should be an honest and truthful one. Labeling is not honest and truthful, and does not comply with the statute, if it does not reveal that there has been added to the orange a substance (assuming it is harmless) which (1) is an artificial coal-tar dye, and (2) is designed to conceal the inferiority of the orange and make it appear better and of greater value than it is.

Respectfully submitted, Chase & Company, Randall Chase, Vincent A. Kleinfeld, Counsel.

1052 Pennsylvania Building, 425 Thirteenth Street, N. W., Washington 4, D. C.

Before the Department of Health, Education and Welfare
Food and Drug Administration

In the Matter of: Color Certification

Docket No. FDC-60.

EXCEPTIONS OF COAL-TAR COLOR INDUSTRY COMMITTEE

The Coal-Tar Color Industry Committee, whose members produce 90% of the coal-tar colors produced in the United States for use in foods, drugs and cosmetics, [fol. 83] make 3 types of exceptions to the proposed order concerning FD&C Orange No. 1, FD&C Orange No. 2 and FD&C Red No. 32 (hereinafter referred to as "Orange 1", "Orange 2" and "Red 32", respectively) published at pages 9352 and 9353 of the Federal Register of December 30, 1954. These types of exceptions are:

1. The basic exception that the order does not comply with the statutory mandate.

Denied.

2. Exceptions for failure to make certain factual findings which are fully supported and wholly uncontradicted by the record.

Allowed in Part. See specific exceptions infra.

3. Exceptions based upon the fact that the proposed findings do not truthfully or accurately reflect the record, and that such proposed findings are incomplete, exaggerated and distorted.

Allowed in Part. See specific exceptions infra.

Basic Exceptions

1. The proposed order is not based on substantial evidence of record as required by Section 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. Sec. 371(c)).

Denied.

[fol. 84] 2. The last paragraph of the Secretary's Proposed Finding of Fact 3, appearing in the first column of page 9353 of the Federal Register of December 30, 1954, should be changed to read as follows (new matter is in italic; deleted matter is stricken through):

"The results of pharmacological tests, conducted by qualified investigators using recognized scientific methods, established that the colors are ~~not~~ harmless substances *in the quantities in which ordinarily used or in quantities in which their use can be reasonably anticipated, but on the contrary are definitely toxic and exert pronounced physiological effects on body tissue. The experimental work on man is limited, and except for Orange 1 adverse effects on man have not been definitely confirmed.*"

Denied. (Findings changed, but substance objected to remains.)

3. In light of the suggestions made above and those made hereafter, Findings of Fact 4 and 5 in the Secretary's Proposed Order are unnecessary and should therefore be deleted.

Denied.

4. Conclusion 1 of the Secretary's Proposed Order should be modified by deleting the word "not" before the word "harmless".

Denied.

5. In Conclusion 2 of the Secretary's Proposed Order, [fol. 85] the word "not" should be inserted between the word "should" and the words "be deleted", and the following matter in proposed Conclusion 2 should be deleted:

"since the Secretary cannot continue to list these colors as colors that the Food and Drug Administration will certify as harmless and suitable for use in coloring food or in coloring drugs and cosmetics intended for other than external application."

Denied.

6. In light of the proposed changes suggested above, Conclusions 3, 4 and 5 of the Secretary's Proposed Order become unnecessary and should be deleted, and the proposed amendment of Part 135 of the Color Certification Regulations becomes unnecessary and should therefore be deleted.

Denied.

II

Exceptions Based Upon Failure to Find Uncontroverted Facts

Exception is taken to the Secretary's failure to make the following findings all of which are fully supported and wholly uncontradicted by the record. (For convenience, the transcript of testimony is hereinafter referred to as "R.")

1. The following tests, with the results indicated, were [fol. 86] conducted by the Division of Pharmacology of the Food and Drug Administration of the government of the United States of America:

(a) Orange 1.

i. In the two-year period 1939-1940, twenty rats were fed on a diet containing 0.1 percent Orange 1. No significant effect on growth or mortality was observed, and no effect was observed in the gross and microscopic examination of the animals (R. 14).

Allowed in Part. See Finding 4.

ii. In the five-year period 1938-1943, three dogs who were fed capsules containing 5 milligrams of Orange 1 per kilogram of body weight per day appeared in satisfactory condition throughout the experiment and were sacrificed at the end of 61 months to terminate the experiment. Pathological examinations of these dogs showed nothing which could be attributed to the color (R. 16-18).

Allowed in Part. See Finding 4.

(b) Orange 2.

i. For a period of two years beginning in 1939, 24 rats were placed on a diet containing 500 parts per million of Orange 2. A second group of 24 rats received the same diet without the added color in a parallel 2 year experiment. Groups of 18 rats were fed 500 parts per million and 100 parts per million of Orange 2 mixed in a low-protein diet, and a third group of 18 rats received the low-protein diet alone:

[fol. 87] Allowed in Part. See Finding 5.

There was no effect on mortality as a result of feeding Orange 2 at these two levels.

There were changes in the hearts of the animals which had received 500 parts per million of Orange 2 in their diet; but only in the case of two animals at the 100 parts per million level was there a suggestion of certain other changes (R. 23-24).

ii. In an experiment begun in 1938 one dog received 100 milligrams per kilogram per day given as an oil solution by a period of about 11 months. Following this the dose was reduced to 20 milligrams per kilogram per day and was continued for 60 months. A second dog was started on 100 milligrams per kilogram per day given as an oil solution by stomach tube for about a month. The dose was then reduced to 20 milligrams per kilogram per day for about a month, and finally to 5 milligrams per kilogram per day administered in capsules. This dose was continued for 62 months:

Allowed in Part. See Finding 5.

In the case of the first dog the dose was reduced from 100 milligrams because the dog was in poor condition as a result of this dose. When the dose was reduced to 20 milligrams per kilogram per day the color was tolerated and the dog gained weight. It was sacrificed in good condition after 60 months on this dose. The dose in the second dog was reduced, first from 100 milligrams per kilogram per day to 20 milligrams per kilogram per day, and finally to 5 [fol. 88] milligrams per kilogram per day, because the dog was not eating well, and was gaining weight slowly on the higher doses. The 5 milligrams per kilogram per day was

tolerated and the dog was sacrificed apparently in good condition after 62 months on this dose.

In this period of time the dog had 6 litters of puppies, which were of average size and health (R. 26-27.)

(c) Red 32.

i. Beginning in 1938, Red 32 was administered to 5 dogs, each of whom received a dose of 5 milligrams per kilogram per day for a period of five to six years. One of these dogs received a dose of 100 milligrams per kilogram per day for approximately a month, a dose which was later reduced to 20 milligrams per kilogram per day for approximately a month. Another dog received 100 milligrams per kilogram per day for about ten months, a dose which was later reduced to 20 milligrams per kilogram per day and continued for approximately five years. All 5 dogs were sacrificed at the end of the five-year period in apparently good condition, though the two dogs which received 100 milligrams per kilogram per day of Red 32 showed moderate weight loss while this dose was being given (R. 35-36).

Allowed in Part. See Findings 7 & 8.

ii. In addition, one of the constituents of Red 32, the para-isomer, was administered to two dogs at a dose of five milligrams per kilogram per day for six years and the meta-isomer was administered to three dogs at a dose of five [fol. 89] milligrams per kilogram per day also for six years. Pathological examinations of the animals following sacrifice showed no changes which could be attributed to treatment (R. 35-36).

Allowed in Part. See Findings 7 & 8.

iii. Experiments in 1940 and 1941 showed that a 0.1 percent concentration of Red 32 in the diet of rats markedly depressed the growth and reduced the median survival time (R. 31).

Allowed in Part. See Finding 7.

2. In its toxicological studies, the Food and Drug Administration attempted to administer the compound under investigation at a series of levels, some of which would produce no effect, some a slight effect, and others a

marked effect. Where the color was given at only one dosage level in the experiment, it would be impossible to achieve all of those ends (R. 42-43).

Denied.

3. The levels at which the dosages were administered in all the tests referred to in the record were not related to the levels of the colors as actually used under normal conditions of use (R. 43).

Denied. See Finding 10.

4. Common table salt could produce harmful effects and a human being would suffer some adverse effects when ingesting 2 or 3 ounces of salt (R. 47-48).

Denied.

[fol. 90] 5. In sufficient quantities any substance might cause adverse reactions (R. 49).

Denied.

6. The amount and conditions of proposed use of a material are necessary data for deciding whether in a pharmacological sense a material is harmless for the use intended (R. 57.58, 60).

Denied. See Finding 10.

7. There is no evidence that Orange 1, Orange 2 or Red 32 would cause harmful effects in quantities used under ordinary conditions of use, except that several years ago a sample of candy containing 700 parts per million (.07 percent) of Orange 1 was collected by the Food and Drug Administration as the result of a complaint that that candy had caused diarrhea in a child. This candy contained 700 parts per million of the dye, an amount greatly in excess of the amount normally used and which constitutes an abuse. Three human volunteers, one of whom ate 6 or 8 pieces of the same candy, one of whom ate 4 pieces and one of whom ate one piece, suffered marked abdominal griping and diarrhea (R. 67-68. 0-21).

Allowed in Part. See Findings 3, 9 & 10.

8. The concentration of dye in color-added oranges ranged from 3.39 to 6.78 parts per million of dye per fruit (R. 101).

[fol. 91] Denied. See Findings 9 & 10.

9. The concentration of dye in the peel of fresh fruit ranged from 17.63 to 34.26 parts per million (R. 101).

Denied. See Findings 9 & 10.

10. The concentration of dye in juice extracted from whole fruit to which color has been added ranged from .04 to .07 parts per million (R. 101).

Denied. See Findings 9 & 10.

11. Candid orange peel had 7.4 parts of dye per million (R. 101).

Denied. See Findings 9 & 10.

12. Orange marmalade had 1.8 parts of dye per million (R. 102).

Denied. See Findings 9 & 10.

13. One of the products produced by Kline & French Laboratory contains Orange 1 to extent of 2 micrograms per recommended daily dose. This is $1/4,000,000$ of the 1,000 parts per million (.1 percent) (see Proposed Finding II 1(a) i., above) fed to rats by the Food and Drugs Administration over a two-year period and found to produce no effect (R. 103).

Denied. See Findings 9 & 10.

14. The 2 microgram per day dosage referred to in Proposed Finding 15 above is $1/200,000$ of the 5 milligrams [fol. 92] per kilogram of Orange 1 fed to dogs by the Food and Drug Administration (see Proposed Finding II 1(a) ii., above) for 62 months and found to have had no effect (R. 103).

Denied. See Findings 9 & 10.

15. Another of the products of Kline & French Laboratory contains Red 32 to extent of 30 to 35 micrograms per

daily dose. This is 1/10,000 of the dose of 5 milligrams per kilogram a day fed to dogs by the Food and Drug Administration (see Proposed Finding II 1(c) i., above) in a 5-year experiment and found to produce no effect (R. 103-104).

Denied. See Findings 9 & 10.

16. The amount of dye used in the Kline & French Laboratory products described in Proposed Findings 15 through 17, inclusive, above, is indicative of the relative amounts of those dyes commonly used in pharmaceutical preparations (R. 104).

Denied.

17. The amount of dye in pharmaceutical products is normally of the order of magnitude ranging from 2 to 35 micrograms per recommended daily dose (R. 105).

Denied.

18. The Food and Drug Administration has taken cognizance of the differing orders of toxicity of coal-tar colors by providing at least 3 classifications for these colors, [fol. 93] namely, FD&C, D&C, and External D&C (R. 104).

Denied.

19. The total weight of a 1408 calory reducing diet is 1172 grams (R. 117).

Denied.

20. The amount of food purchased at retail in the United States per individual in the period 1909-1952 was above 1500 pounds per year in all years but two, where the amounts purchased equalled 1499 and 1494 pounds. This corresponds to approximately 1800 grams of food per day (R. 117-118).

Denied.

21. The average human diet in the United States is between 1 kilogram and 1500 grams per day (R. 118).

Denied.

III

Exceptions Based upon Inaccuracies and Distortions Contained in Secretary's Proposed Findings

While the Committee does not believe that the Secretary's Proposed Findings are relevant or material, if such findings are to be made, the Committee believes that they should honestly reflect the record.

[fol. 94] On that basis, the Committee has set forth in separately-lettered paragraphs below the Secretary's Proposed Findings, striking out the matter which it believes is not supported by the record, and in *italics* matter which it believes must be added to accurately state the record:

A. "Findings of Fact . . . 1. After a hearing held beginning February 6, 1939, . . . (R. 46)"—No exception.

Allowed.

B. "2. Because of advances in knowledge and techniques in the field of pharmacology, the Food and Drug Administration has initiated new tests to explore more fully the toxicity of the certifiable coal-tar colors. This involves the application of all techniques and procedures now considered necessary to assure proper evaluation. A number of these tests, with present-day techniques and procedures, have been conducted by the Division of Pharmacology of the Food and Drug Administration, using FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32."

There is no testimony in the record, aside from the fact that some tests are more recent than others, to support the words stricken above.

C. "Tests that have been terminated are: . . .

"Tests that were still in progress at the time of the hearing were: . . .

[fol. 95] "Tests of the three colors by external application . . . Ex. 2, 3, 4)."

Allowed in Part. See Findings 2-8.

It is proposed that this matter be deleted at this point in the Proposed Finding, and that each test be discussed

separately, together with the results thereof. This will eliminate redundancy, confusion and error. Specific exception, however, is taken to those portions of the Secretary's Proposed Findings which refer to carcinogenicity tests on the ground that such references are immaterial, irrelevant, inflammatory and highly prejudicial, since the record shows the results of those tests were not positive, and on the further ground that in the absence of the added findings -hat the results of such tests were not posi-ive, -he erroneous inference might be made that the colors are carcinogenic (R. 16, 26, 35).

D. "3. The tests that have been concluded are tests normally employed to determine the toxicity of substances taken internally by man. The result of those investigations *the concluded tests* show that each of the coal-tar colors FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32, taken internally, caused marked damage to various vital organs of *the certain rats and dogs used as test animals*, significant changes in body weight, and premature death of such animals when certain large dosages of such colors, as specified below, were administered. Such large dosages were not related to the levels of the colors as actually used under normal conditions of use."

[fol. 96] The matter deleted is unsupported by the record except in those cases where deletion is grammatically required by the change in substance. The added matter makes the phraseology more precise, is in accord with the Exhibits, and is supported by the testimony at R. 43.

Allowed in Part. See Findings 2-8.

E. "FD&C Orange No. 1 caused the premature death of all rats on a diet containing 2.0 percent of the test substance. In rats on a diet containing 1.0 percent of this substance there were marked *retardation of growth*, increased mortality, and chronic congestion and enlargement of the spleen. These same manifestations, to a somewhat lesser extent, were encountered in rats consuming a diet containing 0.5 percent of FD&C Orange No. 1."

In 1951-1953, 24 rats were placed on each of three levels of Orange 1, namely 0.5 percent, 1 percent and 2 percent. A similar group served as controls. The results show that there was a marked adverse effect on growth at the 1 per-

cent level, a slight effect on growth at the 0.5 percent level. There was an effect on mortality at all levels. There was moderate to marked anemia at various times on the 0.5 and 1 percent levels. The pathological examination of the animals showed splenic enlargement at the one percent level, some splenic enlargement at the half percent level, and congestion in various organs at the one percent level. (R. 15-16.)

[fol. 97] Denied. See Finding 3.

F. An experiment began in 1938 and continued until 1943 consisted of administration of capsules containing Orange 1 to dogs. Three dogs received five milligrams per kilogram per day for a period of approximately five years. Two additional dogs received one hundred milligrams per kilogram per day. The dogs which received 5 milligrams per kilogram per day appeared in satisfactory condition throughout the experiment and were sacrificed at the end of 61 months to terminate the experiment. Dogs consuming 100 milligrams per kilogram per day of FD&C Orange No. 1 were in satisfactory condition through the early part of the experiment, but after about two years the dogs began to lose weight and died in 26 months and 33 months. They had occasional diarrhea while alive and manifested terminal weight loss. Diarrhea was noted at the beginning of the experiment in one of the 100 milligram per kilogram dogs, and terminally in another. Autopsy revealed congestion and atrophy of the liver attributable to the test substance. Pathological examination of the dogs showed nothing which could be attributed to the color at the 5 milligram per kilogram per day dose. At the 100 milligram per kilogram per day dose, there were liver changes which consisted chiefly of centrilobular liver congestion and atrophy.

The record, pp. 16-18, fully substantiates the foregoing modification of the proposed finding.

Allowed in Par. See Finding 3.

[fol. 98] G. In an experiment begun in 1951, on a diet containing 1.0 percent of FD&C Orange No. 1, four dogs exhibited chronic diarrhea, rapid deterioration, and weight loss. One dog was sacrificed in extremis at 28 days, and one was found dead after 35 days on the diet. These dogs

had eaten poorly and had lost about 50 percent of their body weight. The remaining two dogs are still surviving. They are maintaining their body weight, and are still on the experiment which has now continued for approximately 24 months. Autopsy revealed muscular dystrophy and testicular and prostatic atrophy. These same manifestations occurred to a lesser extent in dogs on a diet containing 0.2 percent of FD&C Orange No. 1.

Allowed in Part. See Finding 3.

In the same period, four dogs were fed 0.2 percent of Orange 1 in their diet. Of these, one was sacrificed in extremis at 85 days, a second at 260 days. They had lost 37 percent and 45 percent of their body weight, respectively, in spite of having eaten well during the course of the experiment. The remaining two dogs on the 0.2 percent level appeared to be in good physical condition at the end of 23 months on the experiment.

Examination of these four dogs showed such changes as muscular dystrophy in all four, marked testicular and prostatic atrophy in the two males, varying degrees of atrophy in several other organs, bone marrow depletion in 3 of the 4 dogs, and additional changes.

The suggested modifications are supported by the testimony at R. 18-19, 39.

[fol. 99] H. A single dose of 100 milligrams to 200 milligrams of FD&C Orange No. 1 produced diarrhea in most dogs. An experiment conducted in 1952 consisted of administering 200 milligram capsules of Orange 1 to dogs which had been fasted overnight. 11 of 16 animals which were tested developed diarrhea in a period of 4 to 8 hours after receiving the dye. When a dose of 100 milligrams of Orange 1 was administered to 10 of these 11 dogs, 7 responded with diarrhea, two were negative, and one was doubtful. An additional experiment was conducted which 200 milligrams of Orange 1, dissolved in 100 milliliters of water, was administered to 5 of these dogs by stomach tube. All 5 of them responded with diarrhea.

Denied.

The suggested modification conforms to the testimony at R. 19-20.

I. Several human volunteers taking 80 milligrams to 100 milligrams of Orange 1 in a single dose experienced marked griping and diarrhea (see R. 21).

Denied.

J. In an experiment begun in 1940, 10 rats were fed a diet containing a 0.1 percent concentration of Orange 2 for 8 weeks after which the concentration was increased to 0.2 percent. In a succeeding experiment, five rats were given a diet containing 0.1 percent of Orange 2 and ten rats were given a diet containing 0.25 percent of the color. Additional 5 animals served as controls and received a diet without [fol. 100] added color. These experiments indicated that FD&C Orange No. 2 caused severe growth retardation and increased mortality to rats on a diet containing 0.25 percent of the test substance. At 0.2 percent of the rats' diet, there were increased mortality and degeneration of the liver. At a level of 0.1 percent of the substance in the diet, the rats exhibited marked growth retardation. At a level of 0.5 percent, autopsy revealed enlargement of the right side of the heart and slight hypertrophy or hyperplasia of the cells in the liver.

Allowed in Par. See Finding 5.

There is nothing in the Record to support the material stricken; material added makes the Proposed Finding more accurate (R. 23-26).*

K. Five milligrams per week given to rats by subcutaneous injection caused increased mortality and moderate

* While, as previously noted, in these exceptions tests are discussed with their results, it should be noted that the Secretary's proposed findings in discussing tests made of Orange 2, states at paragraph b.ii, at the top of Column 2 at p. 9352 of the Federal Register of Dec. 30, 1954, that weekly subcutaneous injections of 0.1 milliliter of a 5 percent suspension of Orange 2 were discontinued after 8 injections because of toxicity. This is erroneous since only 3 of 18 rats were affected (R. 25-26).

growth retardation. In 1953, 18 rats were given weekly subcutaneous injections with 0.1 milliliters of a 5 percent [fol. 101] suspension of Orange 2 in glycerine. Control animals were injected with glycerine alone. One of the rats which received the color died following 7 injections. A second died after 8 injections, and the injections were discontinued. A third rat was found dead 11 days after the final injection of Orange 2. There were no deaths among the control animals. (R. 25-26.)

Denied.

L. Dogs consuming 100 milligrams per kilogram of body weight per day of FD&C Orange No. 2 lost weight or gained poorly. Twenty milligrams per kilogram of body weight per day caused one dog in the experiment to gain weight poorly.

For an accurate statement of this finding see Proposed Finding II 1(b) ii., *supra*, p. 5.

Allowed in Part. See Finding 5.

M. Dogs In 1953 four dogs were started on a diet containing 0.2 percent of the test substance (Orange 2). They had diarrhea at the beginning of the experiment for the first few days on this diet and exhibited rapid deterioration and weight loss. They ate poorly, lost weight steadily. On the 28th day of the experiment two of the dogs were sacrificed in extremis. They had lost 43 and 32 percent of their initial weight. The remaining two dogs had lost 31 and 21 percent of their initial weight, respectively. They were placed on a normal diet for 9 days, and during this rest period they regained some weight and improved their physical condition. Then with two additional dogs they [fol. 102] were placed on a normal diet for 9 days, and during this rest period they regained some weight and improved their physical condition. Then with two additional dogs they were placed on a diet containing 0.04 percent Orange 2. On this diet, the four dogs did well for about a month. Following this they began to eat poorly and lose weight. At 0.04 percent of the On this diet, the dogs then gradually deteriorated and lost weight, and autopsy revealed atrophy of various vital organs.

The suggested changes are supported by R. 27-28.

Denied.

N. In 1952, a single dose of 200 milligrams of Orange 2 produced diarrhea in five dogs who had previously been found sensitive to the cathartic action of Orange 1.

The suggested changes are supported by R. 27-28.

Denied.

O. When in 1951 FD&C Red No. 32 was fed to rats at a level of 2.0 percent of the diet, all the rats died within a week. At a 1.0 percent level, death occurred within 12 days. When weanling rats were given 0.5 percent they died within 21 days. At 0.5 percent most of the 3 of 5 slightly older rats died within 26 days. At 0.25 percent approximately half of the rats died within 3 months two rats died in 7 and 6 weeks and the remaining 3 were sacrificed at the end of 10 weeks. (R. 31-32.)

Denied.

[fol. 103] P. All the rats showed marked growth retardation and anemia. An experiment in 1952 involved feeding Red 32 in the diet of rats. The results show a marked effect on mortality at a level of .25 percent, a less pronounced effect on mortality at 0.1 percent, and a marked retardation in growth in both groups. Moderate to severe anemia, depending on the dose, and an increase in the white cell count. (R. 33.)

Denied.

Q. Autopsy revealed moderate to marked liver damage at the 0.25 percent level of the diet. Similar but less severe results were obtained with rats on a diet containing 0.1 percent of FD&C Red No. 32. In addition to liver damage, however, autopsy also revealed enlargement of the right side of the heart in this latter group slight to moderate liver damage and heart lesions at the 0.1 percent level of the diet. (R. 33.)

Denied.

R. In 1953, subcutaneous injection of approximately 10 milligrams per week caused death within 8 weeks to most

rats on the experiment per rat resulted in such toxicity that the experiment was discontinued. These rats exhibited anemia, hemorrhage, and reduction in the size of the liver. Neither with respect to Orange 2 nor Red 32 was the experimental test continued long enough to reach any conclusion as to the possibility of carcinogenicity by repeated subcutaneous injection of rats. (R. 34-35.)

Denied.

[fol. 104] S. Dogs taking 100 milligrams per kilogram of body weight per day showed moderate weight loss. See Proposed Finding II 1.(c) i. and ii., *supra*, pp. 6-7.

Allowed in Part. See Findings 7 & 8.

T. A level of 0.2 percent of FD&C Red No. 32 in the diet of dogs caused rapid deterioration and weight loss and sporadic diarrhea; 0.04 percent caused gradual deterioration and weight loss, sporadic diarrhea, moderate atrophy of vital organs, and muscular dystrophy; 0.01 percent in the diet caused weight loss and the death of one out of four dogs. In 1953, four dogs were fed a diet containing 0.2 percent of Red 32. Two of these were sacrificed at the end of 26 days after they had lost 28 and 29 percent of their weight. The other two dogs were placed on a control diet for ten days, and after they had regained weight and improved their condition they were placed with two additional dogs on a diet containing 0.01 percent Red 32. One of the four dogs lost approximately 60 percent of its body weight and was found dead after 173 days on the diet. The remaining 3 dogs lost some weight but appeared to be in fair condition after about 10 months on this diet. Four dogs fed 0.04 percent of Red 32 in their diet lost weight up to about 50 percent and were sacrificed in extremis at 124, 137, and 148 days on the experiment. Sporadic diarrhea was observed during the experiment. Pathological examination showed slight or moderate pallor of the organs and tissues in general, gelatinous bone marrow and atrophy of the liver as judged by gross examination. The principal feature shown by the microscopic examination was atrophy and/or cellular depression of the various organs, such as the liver, [fols. 105-157] spleen, lymphnodes, bone marrow, genital organs, and skeletal muscle. (R. 36-37.)

Denied.

U. A single oral dose of 100 milligrams or 200 milligrams gave diarrhea in the majority of the dogs tested. In 1952, 10 dogs which had previously been found sensitive to the cathartic action of Orange 1 were tested on Red 32. When given 200 milligrams of Red 32, eight of the 10 dogs developed diarrhea. Five dogs were later tested with a dose of 100 milligrams, and four developed diarrhea and one gave questionable results. (R. 37.)

Coal-Tar Color Industry Committee, By Michael F. Markel, Attorney.

Denied.

[fol. 158] Before the Department of Health, Education and Welfare Food and Drug Administration

In the Matter of: Color Certification

21 CFR Part 1535

Docket No. FDC-60

EXCEPTIONS FILED ON BEHALF OF FLORIDA AND TEXAS USERS OF FD&C RED #32 IN THE COLORING OF ORANGES

Pursuant to Notice of Proposed Rule Making in the above entitled matter, heretofore published in the Federal Register, under date of December 30, 1954, the users of FD&C Red #32 in the coloring of oranges, who shipped 12,052,522 boxes, or about 88% of the total color-added oranges in Florida in the 1952-53 season, and the users of FD&C Red #32 in Texas, a list of which appears in the [fol. 159] record, and who previously filed a brief in the hearing, excepts to said Order. Some of these exceptions go to the conclusions and some to the facts stated, or not stated, and some to the Order itself.

Exceptions are made to certain findings of fact, the conclusions and the Order as follows:

Exceptions to Findings of Fact No. 2

1. Said finding of fact is erroneous and makes findings that are not warranted or based upon the record of the hearings.

Allowed in Part. See Finding 2.

2. Said finding of fact recites: "A number of these tests with present day technique and procedures have been conducted, and follows with details of the tests." The record does not show, nor does the subsequent recital in Finding of Fact No. 2 show, any difference between the present day technique and procedures and those employed at the time of the original certification of FD&C Red 132. (R. 8-78) (Exhibit 2, 3, 4). (See particularly R. 12-13 as to General Procedure.) (R. 31-32.) Basis of selection of test levels. (R. 42-43.)

Allowed.

3. In Finding of Fact No. 2, Paragraph (c), subsection iv and v, carcinogenicity tests are mentioned, with the implication that FD&C Red #32 produces Carcinoma. This implication is erroneous and is misleading and without foundation. There is no evidence in Exhibit No. 4 of the hearing [fol. 160] or any other place in the record, substantiating even this implication. (Exhibit 4.) (R. 34-35.)

Allowed in Part. See Finding 2.

4. The test recited in findings of fact No. 2 are unrealistic and have no relationship to the method or manner in which FD&C Red #32 is actually used on oranges. The reported data showed no adverse affect when fed at the lowest levels selected for the purpose of testing, and these levels were in excess of the amount of color likely to be ingested under normal conditions of useage. The details of this will be more fully developed in Appendix A, which is attached hereto and made a part hereof the same as if incorporated herein at this point. (Exhibits 2, 3, 4, 8.) (R. 8-78.)

See Findings 8-10.

5. There is error in the finding of fact and the Order based upon the finding of fact insofar as it relates to FD&C Red #32 for the reason that the record affirmatively shows that tests were made upon two ingredients; namely, para-isomer and meta-isomer. (R. 12), and it is not shown that these ingredients were of satisfactory purity as to freedom from poisonous or harmful substances when they were

received or tested. In fact it is not known and it is not shown from the record, that these ingredients were received from a commercial firm ordinarily engaged in preparing FD&C Red #32.

[fol. 161] Exceptions to Finding of Fact No. 3

6. Said finding of facts recites that the tests are the tests normally employed to determine the toxicity of the substance being taken internally by man, but is erroneous in that it does not show the experimental results on any human beings as to the use of FD&C Red #32; the record showing no experiments on human beings except as to Orange No. 1, and this was under an amount vastly in excess of the amounts ingested under normal conditions of use. (R. 44-45.)

Allowed in Part. See Findings 7-10.

6. (a) The finding "the experimental work on man is limited" is erroneous in that it indicates experimental work as to Red No. 32. The record shows no experimental work on man except a small amount on Orange No. 1 (R. 44-45.) This finding should have recited, to have been correct, "there is no evidence that in the amounts used and in the manner of use in the coloring of citrus fruit, the product so colored is not safe for human consumption".

See Findings 8-10.

7. The finding of fact is erroneous in that it recites that pharmacological tests conducted by qualified investigators using recognized scientific methods established that the colors are not harmless substances.

These findings are erroneous in that it did not take into consideration the uses to which it is put, and the amount which would be ingested under normal conditions of use, the record showing that in the ratio of the amounts fed to the rats and dogs and fed to human beings, it is not harmful to human beings and is not harmful to human beings [fol. 162] in the manner and quantities in which it is used, and the finding should have so recited. (Exhibits 4, 8.) (R. 8-78.)

See Findings 8-10.

The witness, Doctor Vos, on cross-examination, (R. 43-44-45), admitted there had been not a single complaint against FD&C Red #32.

8. The findings in the last paragraph of Finding of Fact No. 3 is erroneous and unsupported by the evidence insofar as it refers to Red #32; the evidence showing that FD&C Red #32 is used exclusively for the coloring of oranges on the outer rind of the orange in infinitesimal amounts (4 ppm) and the tests were not made with reference to the manner of the use or based on the quantities of use to which Red #32 was put. (Exhibit 4, 8.) (R. 42-43.) (R. 101.)

Denied. See Findings 7-10.

Exceptions to the Conclusions and to the Tentative Order as a Whole, insofar as it Relates to FD&C Red #32.

9. The conclusion is erroneous in law and fact in stating that:

Based upon the evidence of toxicity presented at the hearing . . . FD&C Red #32 is not harmless and suitable for use—in coloring food.

Denied. See Findings 7-10. Conclusions 1-4.

This is erroneous in that an erroneous construction has been placed upon the words "harmless and suitable for [fol. 163] use in coloring foods". There is no evidence that FD&C Red #32 is not harmless and suitable for use in the coloring of oranges. None of the amounts used in the tests, including the lowest levels of feedings which produced no injury, bear any relation to the use of these colors likely to be ingested under normal conditions of use. (R. 42-43.)

Exceptions to the Tentative Order as a Whole insofar as it Relates to FD&C Red #32.

10. The finding is based upon tests of materials unidentified as to purity, or place of acquisition, as shown in Exception No. 5.

Denied. See R. 86-88.

11. The record provides no factual basis for an Order amending the coal-tar regulations, so as to delete therefrom FD&C Red #32. (R. 8-78.) (Exhibits 4, 8.)

Denied.

12. The record affirmatively establishes FD&C Red #32 to be harmless and suitable for use in the coloring of oranges, and yet the Order is contrary to this, and is erroneous. (R. 8-78.) (Exhibits 4, 8.)

Denied.

13. The same exceptions as made to the conclusions are made to the tentative Order as a whole. In addition, the finding and determination of the word "harmless" is contrary to the long-established recognition of this word by the Food and Drug Administration and contrary to the [fol. 164] legislative history of the Act. There is no showing in the record of any complaint of the use of FD&C Red #32, or that it is harmful, either in law or in fact.

14. The interpretation now attempted to be placed, and the provision "Be deleted from listing", changes the long recognized interpretation of the word "Harmless" and the original certification made after complete evidence. FD&C Red #32 was certified nearly a quarter of a century ago. No adverse affects have been reported to the Department; and the Order is based upon proposed findings that are incomplete, and fail anywhere in the findings to show particularly that FD&C Red #32 is only being used for the coloring of oranges certified upon the original complete hearing of the Department, found to be harmless and was in common usage prior to the original certification.

Denied.

15. The Order is predicated on an erroneous belief that the Department had to enforce zero-toxicity and could not consider or establish any tolerances or consider the manner in which the dye is used.

Denied.

Respectfully submitted, (S.) J. Hardin Peterson,
Attorney at Law, Attorney for Users of FD & C
Red #32 Named in detail in the original brief filed
in this matter.

Lakeland, Florida.

[fol. 165]

APPENDIX A TO EXCEPTIONS

Dr. Vos Toxicity Tests on FD&C Red #32—Exhibit 4.

Color-added oranges were analyzed by the Food and Drug Administration and also by the Florida Citrus Commission independent of each other, and on entirely separate samples of fruit. Both reported 4 parts per million of Red #32, contained on the basis of the total weight of the fruit. (R. 101.)

Dr. Vos' Reported Experiments:

Experiment #1. Begun in 1940.

Rats fed 0.1 Red #32 in diet showed markedly depressed growth and reduced median survival.

0.1% corresponds to 1000 ppm (parts per million) which is 250-times that found in oranges (of which the peel is not eaten). This is 2.5 times the "100-fold margin of safety" published by Dr. Lehman.

Experiment No. 2. Begun in 1941.

0.1% of Red #32 in diet of rats.

Again 250 times that found in oranges.

Experiment #3. Begun in 1951.

a. Rats fed at 2% level of Red #32 in diet

b. Rats fed at 1% level of Red #32 in diet.

c. Rats fed at 0.5% level of Red #32 in diet.

[fol. 166] This corresponds to:

a. 20,000 ppm or 5,000 times the amount found in oranges.

c. 5,000 ppm or 1250 times that in oranges.

b. 10,000 ppm or 2500 times that in oranges.

Experiment #4. Begun in 1952.

a. 0.10 Red #32 fed in diets of rats.

This is 1000 ppm or 250 times that in oranges.

b. 0.25% Red #32 fed in diet of rats.

This is 2500 ppm or 625 times that in oranges.

Experiment #5. Begun in 1953.

Rats injected with Red #32 periodical in tests for carcinogenicity.

No evidence of car-inoma found per Vos' report.

Experiment #6.

Same as Number 5, but again per Vos' report—no carcinoma found.

Experiment #7. Begun in 1938.

5 dogs fed milligrams of Red #32 per kilogram of body weight per day (mf/kg per day) for a period of 5 to 6 years.

One dog received 100 mg/kg per day for one month and later 20 mg/kg per day for one month.

[fol. 167] Another dog received 100 mg/kg per day for 10 months and then 20 mg/kg per day for the balance of 5 years.

The conclusion of this experiment as reported was "Pathological examination of the animals following sacrifice showed no changes which could be attributed to treatment".

An average dog weighs about 10 kilograms (kg) and eats about 400 grams (about 1 pound) of food per day. Calculations in term of parts per million are as follows:

- a. 5 mg/kg/day is equal to 125 parts per million.
- b. 20 mg/kg/day is equal to 500 parts per million.
- c. 100 mg/kg/day is equal to 2500 parts per million.

These values re respectively 31; 125; and 625 times the amount of dye found in oranges.

Experiment #8. Begun in 1953.

- a. Dogs fed 0.2% Red #32 in diet.
- b. Dogs fed 0.04% Red #32 in diet.
- c. Dogs fed 0.01% Red #32 in diet.

These levels correspond to respective levels of 2000 ppm, 400 ppm, and 100 ppm, or 500; 100; and 25 times the amount of dye found in oranges.

Experiment #9. Begun in 1952.

Ten dogs were fed on empty stomachs 200 mg of #32, in capsules, but with no food, and therefore no dilation whatsoever.

[fol. 168] Mathematically, this is infinity times the 4 ppm found in oranges. It would seem that this test is meaningless.

However, 4 ppm of dye in an orange, amounts to 0.8 mg per orange. Since an average man weighs about 7 times the weight of a dog by comparison, a man would have to be

given (on an empty stomach) 1400 mg of dye. Thus to get this amount by eating oranges, a man would have to eat 1700 oranges at one time and—peel and all.

Before Department of Health, Education, and Welfare
Food and Drug Administration.

Notice of Proposed Rule Making Color Certification.

BRIEF OF INTERESTED USERS OF FD&C RED #32 AND OTHERS
REFERRED TO IN THE BRIEF IN SUPPORT OF EXCEPTIONS TO
TENTATIVE ORDER DATED DECEMBER 22, 1954.

This brief is filed on behalf of Florida and Texas packers and packing houses using a coal-tar color FD&C Red #32 in the coloring of oranges, and are the same parties as appeared and filed a brief by Michael Markel and J. Hardin Peterson, and all are users of this coloring method and many of these are citrus growers, and as growers, are members of the Florida Citrus Mutual, which filed an appearance in the said matter, and are under the regulations of the Florida Citrus Commission, which also filed an appearance in the said matter and are interested parties who will be adversely affected by the tentative Order; the names of the interested parties being shown on the last page of the brief.

[fol. 169] Exceptions Nos. 1 and 2 to Finding of Fact No. 2.

In view of the fact that this brief is attached to the exceptions, for convenience we are not repeating the exceptions verbatim.

These findings are based upon the general statement that there had been an advance in knowledge and technique in the field of pharmacology and that a number of these tests, with present-day's technique and procedures have been conducted. The details of the tests are set forth and appear on pages 8 to 78, both inclusive of the record, and Exhibits Nos. 2, 3 and 4.

The findings are in error and based upon an erroneous assumption. There is nothing in the record to show advance in knowledge and technique or new technique and procedure. No references in the hearings at any place are made to advance in knowledge and technique, or to new methods; to the contrary, a comparison of the methods used in this hearing, and the tests which served as a basis

for the acceptance of the original list of 18 food colors shows that the same methods of tests were used.

The pharmacological tests that served as a basis for acceptance of the original list of 18 food colors are described in a paper entitled "Coal-Tar Colors: Their use in foods, drugs and cosmetics" by Dr. Herbert O. Calvery, former Chief of the Division of Pharmacology, Food and Drug Administration. This paper appeared in the *American Journal of Pharmacy*, Vol. 114, No. 9, pp. 324-349, September 1942. The following three paragraphs are of interest:

[fol. 170] "Fortunately our pharmacological investigations of the fifteen colors on the certified food list and several others, some of which we had had under way for a period of over two years, had been sufficiently extensive to furnish us a basis of evaluation of the new colors. These investigations, using different species of animals, had included: acute tests by oral and intraperitoneal administration; sub-acute feeding experiments incorporating low, medium, and high levels of the dyes in the diets (in some of these experiments the animals were permitted free access to food while in others the "paired feeding" technique was used) and chronic feeding experiments with different levels of the dyes in the diets."

"In light of the early experience with Sudan I and Butter Yellow and in view of other considerations, it was immediately obvious that no new color, however essential it seemed to be, should be added to the list, even with a background of commercial use, until a variety of pharmacological data were available to show its relative toxicity and its harmlessness and suitability for use when compared with the well-known food colors."

"Our investigations consisted of the determination of the acute oral toxicity on rats, the acute intraperitoneal toxicity on mice, and a minimum of sixty days subacute feeding experiments. In these experiments three levels of the dye were fed to different groups of rats, the highest level being sufficiently large in all cases to produce positive results. In addition we tested each of the colors for their effect on the skin of groups of guinea pigs by the technique Landsteiner and his co-workers used in their investigations [fol. 171] of the ability of compounds to cause skin sensi-

tization. They had found that the skin of the guinea pig responds to most chemical compounds in a very similar manner to that noted in man."

There is nothing new between these tests recited and the tests recited in the tentative Order.

Exception No. 3.

~~This exception is based largely on the wording and the fact that it, by inference, may have indicated carcinoma. If mentioned at all, it should have been followed with the finding that there was no showing of carcinoma. The evidence definitely shows this. (Exhibit #4.)~~

Exception No. 4.

We are including in Appendix A, a complete analysis of the method by which the feeding tests were made. These will show they are totally unrealistic and have no relationship to the level or manner in which FD&C Red #32 is actually used on oranges. These tests show that the doses given were given under far different conditions than would have ever been used normally, and that the amount necessary to be taken into a human being would be so great that under no possibility would a human being ever get that amount of the dye.

Exhibit No. 4 shows the nature of the experiments. The testimony shows the high levels at which the tests are made. Using ordinary well known data and reducing the [fol. 172] amount in preparation to the use by humans, we submit a detailed analysis which we attached as Supplemental Sheet A-1 and make it a part of this brief the same as if included herein.

There was a total absence of effort to relate tests to ordinary use level. This is borne out by the testimony of Doctor Vos on page 43 of the record, (R. 43) in which the following questions and answers occur:

"Q. Well then, these levels were not specifically related to the levels of these colors as actually used under normal conditions of use?

A. No, that was not a part of this.

Q. Have you any evidence at such levels where the

capacity for producing harmful effects was tested at levels of ordinary conditions of use?

A. I have very little information on the matter of what the customary levels of use are".

And there is lack of evidence of harmful effects at the levels of ordinary use.

Doctor Vos again on pages 44 and 45 of the record, testified as follows: (R. 44-45):

Question: Dr. Vos, then you have no evidence as to the capability of producing harmful effects of any of these colors at the level of ordinary use under normal conditions of use, I should say.

Dr. Vos: Without having more thorough information on the actual level of ordinary use, I would hesitate to answer that question.

Question: Well, you have no evidence at levels other than the levels appearing in the exhibits.

[fol. 173] Dr. Vos: That appear in the exhibits, that is correct."

Also see page 42 and page 43 of the record. (R. 42-43) with reference to basis for selection of test levels.

Exception No. 5.

There is no Showing of the Purity of the Ingredients Tested. We respectfully feel that there is such an important question on this one phase, that new tests should be made entirely on FD&C Red #32.

Doctor Vos testified (R. 11-12 as follows):

"Q. Has the Division of Pharmacology also carried out experimental work on FD&C Red 32?

A. That is correct.

Q. What was the source of the color used in these experiments?

A. All of that color was obtained from the same source as the preceding two, with the exception of two ingredients known as para-isomer and meta-isomer. These were obtained directly from a commercial firm.

Q. Is that a commercial firm ordinarily engaged in preparing FD&C Red 32 for use in foods, drugs and cosmetics?

A. I don't know".

The record does not show what source the two ingredients were obtained; does not show that the components had a satisfactory purity as to freedom from poisonous or harmful substances; that the witness didn't know whether they were received even from a commercial firm that was ordinarily engaged in preparing FD&C Red #32 for use. [fol. 174] Certainly when tests are made, it is important that the ingredients used in the tests should be free of poisonous or harmful substances and should be of known purity; the source from which they came should be definitely established; even the containers in which they are received and in which the tests are made are important in arriving at a fair test and to seek to withhold from an industry the use of a dye previously found to be harmless by the Food and Drug Administration after extensive tests and base this withholding upon analysis made of ingredients from which we do not know and the record does not disclose and the witness himself didn't know, is a most serious matter, and we respectfully submit that we feel this one thing in itself is important enough to cause the entire matter to be referred back for further study as to FD&C Red #32, and to have the Honorable Secretary withhold her approval of the final Order.

Exceptions as to Finding of Fact No. 3.

The finding recites that the tests that have been concluded are the tests normally employed to determine the toxicity of substances taken internally by man, and that pharmacological tests conducted by qualified investigators using recognized scientific methods established that the colors are not harmless substances.

Examination of the record will show that there is no evidence to the effect that FD&C Red #32 is harmful to human beings. In fact the record does not show any tests made on human beings of FD&C Red #32. The record shows clearly that the only tests made on any human beings was with reference to FD&C Orange #1. (R. 20-21.)

[fol. 175] The record (R. 128-129) shows that the sale of FD&C Red #32 has been discontinued for any other purpose than the coloring of oranges.

Doctor MacDowell, in his testimony (R. 1.01) and Exhibit 8, shows that juice extracted from color added oranges contained from .04 to .07 ppm (parts per million) of dye. This shows clearly and the analysis attached as A-1 shows the absurdity of claiming that it is harmful to man. Such being the case, its use in the coloring of oranges should not be prohibited.

As late as in 1950 the Food and Drug Administration, in the matter of Violet No. 1, did not apply a strict definition of "harmless" or say that it was harmless. They said:

"The amount of color fed to animals in the tests referred to in Finding No. 12 was far in excess of the amount that any human might obtain as a result of food colored with FD&C Violet #1."

(Finding of Fact No. 12. Federal Register, Vol. 15, No. 109, Page 3517, June 7, 1950.)

The witness, Doctor Vos, stated on page 63 of the record (R. 63):

"The Witness: *I think it is appropriate the method of use should be taken into consideration.* The dyes in question are at present being certified for use in foods, drugs, and cosmetics, and the data which we presented in these exhibits have shown that they are not harmless for use in all of those products. As I have pointed out, we have no [fol. 176] data as to whether they are or are not harmless for external application." (Italics ours.)

And on Page 62 of the record, the witness, Doctor Vos said:

"Yes, the amount of dye, of the color has to be considered in determining whether or not it is harmless."

And on Page 57 (R. 57), Doctor Vos also said:

"Q. Dr. Vos, aren't the amount and method of proposed use of material necessary data for deciding whether the material is harmless for the use intended?"

"A. May I hear that question again, please?"

(Question read.)

The Witness: I would say yes."

Exceptions to Conclusion and to the Tentative Order as a Whole

Exception to Nos. 9 to 15 Both Inclusive

Exception No. 10 is to the general Order and has been previously argued. We take the position that the tests of FD&C Red #32 were not correct. It is not shown clearly the source of material, nor whether it was of sufficient purity to be tested. If the test is erroneous, the Conclusion and the Order itself would be erroneous.

[fol. 177] The Conclusion and Order being based upon the alleged evidence of toxicity and the finding that FD&C Red #32 is not harmful and suitable for use in coloring of food will be argued together, for convenience.

From reading the record and reading the tentative Order, we feel that the Conclusions and the Order are based upon an erroneous assumption and construction of the word "harmless". This construction attempted in this Order is different from that which has been used by the Food and Drug Administration for many years. It is different from the Congressional intent. In the previous brief we quoted rather extensively from the legislative history. It was never intended by Congress to have the word "harmless" construed as zero-toxicity.

It is interesting to note that the testimony on the safety of use at the 1939 hearings was presented by Doctor Herbert O. Calvery, a former Chief of the Division of Pharmacology, F. D. A. Doctor Calvery related how he had conducted both acute and long term studies and had administered the products by mouth, by skin contact and by intraperitoneal injection, and using at least three species. He testified:

"We have been engaged in our laboratory for a period of approximately three years in the study of the toxicology of dyes".

(USDA FD&C #4 February 7, 1939. Page 228.)

Among other things he said:

"On p. 233 there is an interesting passage.

Q. "Are there in your opinion any coal tar colors that are harmless and suitable for use in all kinds and classes of Foods, Drugs and Cosmetics."

[fol. 178] A. (Dr. Calvery). "No, in my opinion there are no coal tar colors that are harmless and suitable for use in all kinds and classes of Foods, Drugs and Cosmetics." ...

On p. 243 he states: "Fifteen colors formerly used and certified as food colors. They have been in use for a number of years, and so far as we are aware there is no harm that has come from their use.

"Again on page 243:

Q. "What do you mean by the terms that you have used, harmless and suitable for use? The use to which the color is to be subjected?"

A. "Yes, by harmless and suitable for use for purposes indicated, we mean that in the concentrations that these substances are used for coloring purposes, it is our opinion that no harm can come from them to the user when used in the concentrations for which they are designed and for the purposes for which they are designed" ...

"Q. In considering the amount used, does the tinctorial property of these coal tar colors have some bearing on the amount used?

"A. "Yes, the tinctorial properties of the coal tar colors is such that when they are used in foods, drugs and cosmetics they are used in relatively small percentages, and one takes that into consideration when one speaks of the toxicity of these substances assumed as harmless and suitable for use in drugs and cosmetics." ...

"Q. "Dr. Calvery, how do you arrive at percentage of color which should be allowed as harmless and suitable for use in foods, drugs and cosmetics?"

[fol. 179] "A. "We arrived at the conclusion that we have concerning the use of these from our conferences with the cosmetics, food and drug manufacturers, and after learning from them what the percentages are which in most cases are a fraction of a per cent, we based our reasoning on that premise. The colors are not certified for use as colors to be consumed as colors. They are certified—at

least we are permitting the listing of these for certification—on the basis of the fact that they will be used as we have been told they are being used at the present time, that is, in small percentages.” . . .

“Q. “Now, have you reached an opinion as to the maximum percentages of coal tar colors which would be allowable respectively in foods, drugs and cosmetics, in view of the tolerances for impurities which have been established in these present regulations?”

A. No, we haven't reached a definite conclusion as to what is the maximum that may be permitted. It is our understanding as I pointed out before that these colors are used in relatively small amounts, in most cases only a fraction of a per cent in the finished product. . . .

—if manufacturing processes and the use of these colors should change to such an extent that more than these amounts should be used, on which we have actually taken into consideration in considering the toxicity of these colors, if that should change to an extent whereby larger amounts would be used, I think there would be no question but that we would have to take that into consideration in order of time and consider amendments to the present regulation.”

In an article by Doctor Herbert O. Calvery, which is headed: “Coal-tar colors—their use in Food, Drugs and [fol. 180] Cosmetics, by Herbert O. Calvery, Division of Pharmacology, Food and Drug Administration, Washington, D. C. September 1942, Page 326, Amer. Journ. Pharm., the reference is used:

“Used in foods were harmless in the quantities employed.”

And, in another place the words: “Free from harmful constituents.”

And, on Page 329, the words: “Which might render such foods injurious to health”.

It includes on Page 330, etc. “The selection and rejection of coal-tar colors Under the Act of 1906”.

On Page 334, he states: “Fortunately our pharmacological investigation of the fifteen colors on the certified food list . . . had been sufficiently extensive to furnish us a basis of evaluation of the new colors. . . .”

He gives somewhat in detail the type of experiments which bears out what we have heretofore said, that the

technique used then are the same as used today, and on Page 337 he makes the statement, which we feel is correct, that the Department has certain discretion, has the right to fix tolerances and to consider the methods under which it is used. He used these words, in referring to the Act of 1906, and to the Act of 1938:

"The development of the system of certification for coal-tar colors was a precedent that laid the ground-[fol. 181] work for other and more effective control measures . . . It was the forerunner of the present system of certification of coal-tar colors; under it were set the first tolerances for heavy metals . . ."

What is said above is borne out also by Doctor Campbell in the hearings on the Food and Drug Act in the 1935 hearings. (Senate Hearings S5 Page 59.) That zero-toxicity could not be expected was recognized by Doctor Campbell. He stated:

"There are very few things, as an illustration, in which you will not find contaminating products in some small degree. With our industrial development, it is *extremely difficult to acquire absolute purity in the production of our food supply.* (Italics ours.)

And on Page 60 of the same hearings, he said:

"Now, under the terms of the present law and under the terms of this measure as I have read it so far, action would be authorized in such cases only when the amount of that added deleterious ingredient was sufficient to injure health. There is a complete exclusion of added deleterious ingredients by this section, except where necessary in the production of the product or where unavoidable. In those instances the poison will be permitted or tolerated in amounts corresponding to the need of using the poison, or its unavoidability, in each particular food. The total of the amounts so allocated will not be enough to jeopardize health . . ."

Thus it will be seen that a practical definition of the word "harmless" should be used; that the Congress itself [fol. 182] knew that the colors could not be 100% pure; these administering the Act and sponsoring the Act knew this.

Subparagraph (b) of Paragraph 346 USCA Title 21, by its subheading indicates that those grouping it reached the same conclusion because the subheading is:

"346. Tolerances for Poisonous ingredients in Food and Certification of coal-tar colors for food. Regulations for Tolerating Unavoidable Poisonous Ingredients".

Senator Copeland, who was Chairman of the Committee on Commerce when the hearing was being held in 1935, recognized this also. When reference was being made to spell out tolerances regarding certain ingredients in cosmetics, Senator Copeland said: (Senate hearings 35 Page 39.)

"Senator, Copeland: Well, of course, that is covered by the general term that it should be deemed to be adulterated if it bears or contains any poisonous or deleterious substance which may render it injurious to health. So the Department itself would have to determine whether there was too much of this or that poison in the cosmetic, if there is any there".

The fact that the Food and Drug had discretion in coal-tar matters is also borne out in pages 318 and 319 of the hearings in a colloquy between Senator Copeland and Doctor Harrison and the words "Harmful to health" are used. On page 318 Senator Copeland said:

[fol. 183] "Senator Copeland: Is back of this the thought that these coal-tar colors might be harmful to health?"

"Doctor Harrison: I think there is back of this original phrase the thought that coal-tar colors might be harmful to health".

And then when the question came out to clarify it, it is pointed out, page 319, that the "certification would be in accordance with regulations".

Certain phrases of the interpretation of the word "harmless" as shown by the legislative history and legal decisions thereon will be shown later in this brief.

The Record Provides no Factual Basis for an Order Amending the Coal-Tar Regulations so as to Delete Therefrom FD&C Red #32.

Section 135-3 listing "straight colors" for certification for use in food includes FD&C Red #32. The deleting

of FD&C Red #32 would deny the further use of this color for the purpose of coloring citrus fruits.

The sole record basis in support of the proposal, as stated, is the testimony of Dr. Dert J. Vos (R. pp. 8-78, inc.). This testimony includes a report of ten pharmacological studies carried out by feeding Red 32 to the number and kind of animals as appears in detail in this testimony and in Exhibit 4. There is no need, for present purposes, to analyze each of the experiments reported. This becomes particularly unnecessary since Dr. Vos has stated, on the one hand, that the levels fed to the test animals, in conducting the experiments which he reported, bore no relation whatever to the level of the dye likely [fol. 184] to be ingested by humans under ordinary conditions of use (R. p. 43), and that he had no evidence of the capability of the color to produce harmful effects at levels likely to be ingested under ordinary conditions of use (R. pp. 44-45), and, on the other hand, that the amount of the dye and conditions under which it is used are essential factors in determining whether or not it is harmless (R. pp. 57-8, 62).

The witness concluded his direct testimony by stating that it was his opinion that Red 32 "is not a harmless coal-tar color", without explaining how he arrived at that conclusion (R. p. 38). However, later the witness defines his term "harmless" by saying: "I have said that these colors are not harmless in the sense that they did cause harm to the experimental animals in the experiments which are listed here". (R. p. 67.) Thus it becomes apparent that he arrives at his conclusion of "not harmless" by ignoring his own criteria for establishing harmlessness, namely, the level likely to be ingested under normal conditions of use. This conclusion also ignores the basis for determining harmlessness by the witnesses and by the then Secretary's findings when Red 32 was originally placed on the list in Section 135.03, as being "harmless and suitable for use in food." (F.D.C. Docket No. 9; see particularly Findings 21, 22, and 25 of Order dated May 4, 1939, Federal Register for May 9, 1939, p. 1924.) There is no evidence in the record now before the Secretary which overcomes the evidence and considerations

on the basis of which Red #32 was thus listed for certification.

The only other basis for the conclusion of "not harmless" of Red #32, as stated by the witness, is his state-[fol. 185] ment that, in determining harmlessness of a substance, its potentiality for producing harmful effects should be compared to such potentiality of substances known to be poisonous and generally regarded as such. When pressed for such a comparison, carbolic acid was selected as such a substance (R. pp. 49-51). On more detailed questioning as to the soundness of this comparison the witness admitted that carbolic acid was considered to be a poison—"not harmless"—on the basis of its acute oral toxicity, or LD 50, and its effect on the skin (R. p. 73). However, the witness also admitted on the basis of his own knowledge that the acute oral toxicity of Red 32 was "much less" than that of carbolic acid and that Red #32 had no adverse effects on the skin (R. p. 77). Obviously, this comparison, if sound, then affirmatively established Red #32 as not being a poisonous substance, hence safe or "harmless"; if, on the other hand, the comparison is unsound (from the witness' standpoint the more charitable view), then it still fails to furnish a basis for the stated conclusion, since the record contains no other evidence of the acute oral toxicity and potentiality for harmful effects of known poisons.

It is submitted, therefore, that the record, and particularly the considerations by the witness on the basis which he expressed his conclusions of "not harmless", as summarized, fails to establish a legal basis for amending the coal-tar color regulations as proposed, since the witness' own criteria for establishing this ultimate fact fail to support his conclusion and since Section 406 (b) does not contemplate a determination of the fact of harmlessness on the basis of any of the criteria relied upon by the witness.

[fol. 186] Section 406 (b) is mandatory in its provision. It provides that the Secretary "Shall promulgate regulations providing for the listing of coal-tar colors which are harmless and suitable for use in food, and for certification of batches of such colors." This language contemplates a determination of harmlessness and suitability under normal conditions of use, including the quantity of a

substance which is likely to be ingested under such conditions. The regulations now sought to be amended were obviously established and promulgated on the basis of such a concept. Nothing has happened since then nor does the record contain any evidence suggesting otherwise.

The suggested basis for determining harmlessness also squares with the concepts generally accepted by experts. When pharmacologists and toxicologists approach a question as to whether the substance is harmless or not, the very first question they wish answered is the proposed level of use and the extent of use. Such questions can only imply that harmlessness and suitability of food ingredients, including coal-tar colors, can be determined only when related to specific conditions, including manner and quantity of use. They do not approach the determination of this question by considering all possible abuses which might cause some injury under some conditions of abuse. Dr. Vos' testimony on cross-examination supports these general statements of accepted scientific concepts in evaluating harmlessness of substances intended for food uses.

Intent of the Word Harmless

The succeeding discussion dealing with the Legislative history will show that the word "harmless" should be construed in connection with the entire Act. I am not unmindful of the fact that certain of the provisions of the food, drug and cosmetic Act specifically provide for tolerances, and while no specific rule is spelled out for tolerances in sub-section (b) of Paragraph 346 U. S. Code Annotated, the Secretary is authorized to promulgate regulations, and the whole purpose of the act seems to be that when good manufacturing practices cannot avoid there being some poison, the test is "as he finds necessary for the protection of public health". Tolerances are allowed for residuals in apples, peaches, cherries and other fruit on which it is known that the outside peeling or rind will be eaten, and in some instances must be eaten. Certainly we cannot assume that Congress, which specifically recognized the coloring of oranges, should expect less consideration for a color that is placed outside on the rind when the rind is not eaten and only in extreme instances an infinitesimal amount might get into the juice or in the marmalade, so its

undoubted purpose was to consider the use of the word "harmless" in the manner in which the particular coloring matter is used.

A discussion of the general rules of statutory construction is set forth at 410 and 411 of 50 American Jurisprudence with the supporting cases, and the following are some of the rules which are well supported.

"It is clear that words may not be given a distorted or strained meaning to satisfy the demands of a strict construction."

"A construction which would render the subject to the rule of strict construction is nevertheless entitled to a reasonable, sensible, and fair construction".

[fol. 188] "A construction which would render the statute absurd or unreasonable, is also to be avoided".

"A statute which is subject to the rule of strict construction is nevertheless entitled to a reasonable, sensible, and fair construction".

"The Courts should take a common sense view of the statute as a whole."

"Captious objections, and even the demands of exact grammatical propriety, should be disregarded". (30 American Jurisprudence Pages 410 and 411.)

"The construction must be reasonable. It is a well recognized principle that the law is not concerned with trifles. The doctrine of *de minimis non curat lex* is well recognized." (See *United States v. Hocking Valley Ky. Co.*, 194 Fed. 234, N.D. (1911) On the subject of *de minimis* see also *Bristol-Meyers Co. v. Lit Bros.*, 536 Pa. 81, 6 A. 2d 843 (1949); *National Labor Relations Board v. Bowell Portland Cement Co.*, 106 F. 2d 198, C.C.A. 9th (1939); and *Willson v. Kable*, 177 Va 668, 15 S.E. 2d 56 (1941)" (p. 16, Note 33).

In the various cases that have gone to the Courts of Appeals and to the Supreme Court we find the use again and again of words

"Injurious to health"

"Endanger health"

"Deleterious"

[fol. 189] "Not deleterious to health"

"To safeguard the public health"

Not one has ever contended that the use of the coal-tar colors which are now being studied, have ever been injurious to a human being or will become injurious in the normal use to which it is put in the coloring of oranges. It cannot injure the health of an individual and it will not cause ill effects in the manner in which it is used.

Some of those cases were under the old 1906 Food and Drug Act, but the general principles still apply.

In the *Lexington ton Mill and Elevator* case, 202 Federal at page 615 in which the Circuit Court of Appeals reversed the District Judge, the opinion of the Court, among other things, said:

"The trial Judge decided that if the added substance was qualitatively poisonous, although in fact added in such minute quantity as to be non-injurious to health, it still fell under the ban of the statute, . . . There is no warrant in the statute for such strained construction. The object of the law was evidently:

- (1) To assure to the purchaser that the article was what it purported to be and
- (2) To safeguard the public health by prohibiting the inclusion of any foreign ingredients deleterious to health."

(Citing *Hall-Baker Grain Company vs. U.S.* 198 Fed. 614.)

[fol. 190] Page 621 of the opinion is very enlightening and it shows the fact that poisons in some greater amounts are frequently present in potable water, bacon, ham, fruits, and certain vegetables, etc. It refers also to "the deleterious effect intended to be prevented by the act".

This case went to the Supreme Court of the United States and in the opinion the Court upheld the decision of the Circuit Court of Appeals, and among other things, said:

"It is evident from the charge given and request refused that the trial Court regarded the addition to the flour of any poisonous ingredient as an offense within this statute, no matter how small the quantity and whether the flour might or might not injure the health of the consumer. At least such is the purport of the part of the charge above given and if not correct it was clearly misleading, notwith-

standing other parts of the charge seemed to recognize that in order to prove adulteration it is necessary to show that the flour would be injurious to health. . . . If it cannot by any possibility where the facts are reasonable considered injurious to the health of any consumer, such flour, though having a small addition of poisonous or deleterious ingredient may not be condemned under the act. . . ."

The evidence in the case does not present a disputed issue of fact, but rather a difference between chemists over the meaning of the words "deleterious ingredient, injurious to health"—In recognizing that a small quantity of arsenic is not injurious to health, the government acknowledges that this term is a relative one. Arsenic is found in [fol. 191] infinitesimal quantities in so many articles of feed that it has been said that the air we breathe, the water we drink, the smoke and dust we inhale, and all the foods we consume contain arsenic. If the terms be an absolute one, then they would all be condemned. The quantity of arsenic found in this coloring material is so infinitesimal that, when diluted as it is ordinarily used, it would take years to produce 'a dose' such as is ordinarily prescribed by physicians—one-thirtieth of a grain. In other words, one would be required to drink 150,000 bottles of soda before he would have consumed a quantity of arsenic sufficient to equal the 'dose'.

It may be true that by further process the amount of this drug can be reduced, but complete elimination is impossible. The Congress has not assumed to define with absolute particularity what is or what is not injurious, and we cannot accept the testimony of the one witness who testified for the government to the effect that the word 'injurious' is an absolute term. Rather do we conclude upon the testimony before us that the arsenic present in the quantity disclosed was not injurious".

In this case also the Court stated the purpose of the Act was:

"The purpose was (1) to protect purchasers from injurious deceits by the sale of inferiors for superior articles, and (2) and to protect the health of the people from the sale of normally wholesome article to which have been

added substances poisonous or detrimental to health" (C.A. 7th Circuit, 286 Fed. Rep. Page 84.)

[fol. 192] In the case of United States v. 1950 boxes of Macaroni, although this was an actual adulteration case and it was shown that the addition was poisonous, the Court pointed out:

"It is the duty of the Court to give a fair and reasonable construction of the accomplishment of its object, that object is the exclusion from Interstate Commerce of Fruit products so adulterated as to endanger health" (U.S. vs. 1950 Boxes of Macaroni, 181 Fed. 427.)

At other places in the opinion the Court uses the following words:

"As to the term poisonous", let me state that everything that contains poison is not poisonous. It depends upon the quantity and the combination. A very large majority of the things consumed by the human family contain, under analysis, some kind of poison, but it depends upon the combination, the chemical relation which it bears to the body in which it exists as to whether or not it is dangerous to take into the human system".

This case also sets forth the purpose to protect the public health from possible injury by adding to articles for food consumption, poisonous or deleterious matters which might render such articles injurious to the health of consumers. (Lexington Mill and Elevator Co., 232 U.S. 399; 58 Law/Ed. 658.)

It is interesting to note that the Circuit Court of Appeals pointed out the significance of the fact that no injurious effect had ever been observed. In our case none has ever [fol. 193] been observed. No one claims it will occur to a human being under normal usage. The Circuit Court of Appeals in its opinion in the Lexington Mill and Elevator case, 202 Federal Reporter, 615, just cited, cited the case of W. B. Wood Manufacturing Company v. United States (see C.A. 7th Circuit, 286 Federal Reporter, p. 84, which was a coloring case under the old Act which prohibited the addition "of any poisonous or other deleterious in-

redient which may render such article injurious to health".

In this case it was definitely established there was arsenic in the color, but notwithstanding this, the Court said:

"(2) We are not satisfied, however, that arsenic in such quantity as to be injurious to health was present. The government recognized the impossibility of eliminating arsenic entirely. In fact, the testimony shows that the elimination of arsenic would be at most but a matter of degree. The government certifies color when arsenic is present, and when only slightly less than that found in the confiscated product.

In the case of United States vs. Washington Dehydrated Food Co., 89 Federal Reporter 2d Series, 606 (Circuit Court of Appeals 8th Circuit) which case dealt with apple chops which had been made of apples that had been sprayed with arsenic of lead and a small residue of the spraying compound had remained on the apples after washing and had been carried over into the apple shops, the Court said this:

"The Government's experts were of the opinion that even infinitesimal amounts of these poisons contained in [fol. 194] food might, if a food was regglarly eaten during a considerable period of time, produce in some consumers chronic lead or arsenic poisoning, while the claimant's experts were not in accord, and expressed the belief that lead and arsenic were largely insoluble and in the gastric juices, etc".

The Court further in the opinion said:

"It is noted in this connection that no expert who testified upon the trial was able to say that he knew of any case of lead or arsenic poisoning resulting from eating apples which had been sprayed with arsenic of lead, or the products of such apples."

The District Court below rendered Judgment for the claimant and the Circuit Court affirmed his judgment and held there was no such adulteration as contemplated by the statute.

In the case of *French Silver Dragee Co. v. United States*, 179 Federal 824, the Court pointed out that the act uses such words as "false," "misleading", "deceit," "poisonous", "deleterious" and says:

"Indeed a careful examination of the whole and clearly shows that its object is, as already indicated (1) to prevent deceit and false pretenses in the sale of food and drugs, and (2) to safeguard the public health."

The case further states with reference to the interpretation of the statute:

"The general language should not be so construed to [fol. 195] ruin a legitimate business and yet remedy none of the evils the statute was designed to remove."

In the language of the Supreme Court of the United States in *Holy Trinity Church v. United States*, 143 U.S. 457, 459, 12 Supreme Court 511, 512, 36 Law Ed. 226:

"It is a familiar rule that a thing may be within the letter of the statute and yet not within the statute because not within the spirit nor within the intention of its makers."

"This is not the substitution of the will of the Judge for that of the Legislator, for frequently words of a general meaning are used in a statute, words broad enough to include an act in question, and yet a consideration of the whole legislation or the circumstances surrounding its enactment, or the absurd results which follow from giving such broad meaning to the words, makes it unreasonable to believe that the Legislator intended to include the particular Act. (*Holy Trinity Church vs. United States*, 143 U.S. 457, 459, 12 Supreme Court 511, 512, 36 Law Ed. 226.)

The Supreme Court of the United States in concluding the case just above recited used this language:

"It is the duty of the Courts under those circumstances, to say that however broad the language of the statute may be, the act, although within the letter, is not within the intention of the legislature, and cannot come within the statute."

[fol. 196] It follows from a consideration of the Legislative History and the evidence that the record fails to establish a lawful basis for deleting Red 32 from the list.

of colors as listed in Section 136.3 of the Regulation, in that there is no evidence of record that this color, when ingested in the quantities likely to be ingested under normal conditions of use is capable of producing any harmful effects. Therefore, we say the showing is that under such uses it is "harmless". On the contrary there is affirmative evidence that it is clearly not capable of producing any harmful effects when used for the purpose of coloring oranges, the primary and virtually exclusive use of this color.

The suggestion that normal conditions of use of a color is the proper criteria on the basis of which harmlessness and suitability for use is determined for the purpose of the provisions of Section 406 (b), is also supported by the legislative history of this provision of the law.

Legislative History

In considering the legislative history of Sections 402 (c) and 406 (b) one should start with the related provisions of the Food and Drugs Act of 1906. Their practical administration prior and up to the enactment of the Federal Food, Drug and Cosmetic Act of 1938 should also be considered.

Doctor Campbell at the hearing on S. 1944, Dec. 7 and 8, 1933, used this statement:

"These regulations established the practice of examining [fol. 197] and certifying the *purity and safety* of coal-tar colors as a method for the protection of the public.

It is desirable that it be continued. In this language we are asking for legislative confirmation of a practice which has existed since 1907: (*Italics ours.*)

The Committee Report accompanying S. 5 (Senate Committee Report No. 361, 74th Congress, 1st Session, and set forth in full in our original brief used in these words:

"Under this procedure those colors which were *demonstrated to be without adverse physiological action, and which from a technical standpoint were suitable for use as food colors, were admitted to certification.*"

"Individual batches of these particular colors were then certified by the Department after examination which

demonstrated their freedom from toxic impurities. This has resulted in an adequate supply of harmless colors for all food uses and has operated to the satisfaction of the industry.

You will note here that the Senate Committee construed as "harmless" "those which were demonstrated to be without adverse physiological action".

On the same Bill the House Committee Reported:

"Subsection (b) of this section specifically authorizes the listing of harmless coal-tar colors for use in food and the certification of batches of the listed colors which are found to be sufficiently free from impurities to be safe. This [fol. 198] *continues in effect a system of certification which has been followed almost from the beginning of the enforcement of the old food and drug law in order to make available to the food manufacturing industries adequate supplies of colors of established safety and purity. (Italics ours.)*

Record affirmatively establishes Red #32 "Harmless" and suitable for use in coloring Oranges.

Aside from the general considerations with respect to the use of Red #32 in foods generally, the record affirmatively establishes this color to be "harmless and suitable for use" in coloring oranges. Therefore any amendment of Section 135.3 of the regulations should be qualified so as to continue listing Red #32 for certification for this purpose, in any event.

It has been suggested that the Secretary lacks the statutory authority to establish a list of colors on the basis of specific food uses. This suggestion must be rejected as untenable for reasons, among others, that it is wholly inconsistent with prior practices of long standing and later continued in the administration of Section 406(b). The Secretary has obviously considered conditions of use as a criteria for listing coal-tar colors for certification, because that is the sole basis for the establishment of different classes of colors for certification as "harmless and suitable for use."

Intended use is the basic premise upon which classes FD&C, D&C; and Ext. D&C respectively, have been estab-

lished. Such is also the basis for the provisions of Section [fol. 199] 135.3(c) restricting the "lakes" of water-soluble straight colors of the FD&C list to the use of "external application to shell eggs." The same basic principle was obviously the basis for deleting "Violet No. 1 from the "D&C" list and including it in the FD&C list by Order dated June 1, 1950. The transfer of this color from the more restrictive list to the broader list is rested, in the pertinent findings of fact made in support of that Order, on the ground that the color listed for FD&C certification contained "less impurities" than formerly when it was restricted to the D&C list (Federal Register for May 11, 1950, Findings 7, 8, and 9, p. 2814).

The particular specifications for each color listed for certification, themselves, are determined on the basis of such consideration. Thus, colors which may not meet the desired degree of purity for food uses may, nevertheless, be used in drugs, and those which do not meet the required degree of purity for drug uses may, nevertheless, be used for drugs and cosmetics intended for external use. That same basic principle is also the basis for the separate treatment of coal-tar colors in the food law (Sec. 406(b)), the drug law (Sec. 504), and the cosmetic law (Sec. 604), respectively.

Any criteria other than specified uses would make no sense for, under any other criteria, a color would have to be rejected for all food uses just because it was found unsuitable for use in a single food. This would be clearly inconsistent with all prior administrative practice.

[fol. 200] The administrative practice of establishing classes of dyes on the basis of the intended use of the dye and of restricting it to such use has prevailed for nearly a half century and, as is clear from the legislative history outlined herein, was expressly recognized by Congress in enacting Section 406(b). Under these circumstances the doctrine of "Congressional reenactment" is particularly applicable to any consideration of interpretation of Section 406(b). It is well established that reenactment of a statute is an implied legislative approval of administrative interpretations which may give the interpretations the force of law (See Davis on Administrative Law, 1951, Sec. 59, and cases cited).

It follows, therefore, that the Secretary may, and should continue to certify Red 32 for use in coloring oranges unless the record before her affirmatively establishes, by substantial evidence, that Red 32 is not "harmless and suitable for use" in coloring oranges. As stated, the record not only fails to establish any such thing, but it affirmatively establishes the contrary.

Reference is made to Appendix A and to Supplemental Sheet No. A1 attached hereto which shows clearly that it is harmless in the use for coloring oranges.

Conclusion

FD&C Red #32 is absolutely essential to the continuance of the Commercial practice and economically indispensable in the coloring of oranges. Thus far no other color has been developed.

[fol. 201] We respectfully submit as Doctor Vos said, and it appears heretofore in the brief, but we are using this in the summary.

"I think it is appropriate the method of use should be taken into consideration" (63)

"Yes, the amount of dye has to be considered when it is determined whether or not it is harmless." (62)

On Pages 44 and 45 he said he had no evidence as to the capability of producing harmful effects at the level of ordinary use, under normal conditions of use.

On the same pages he said that the tests were not at levels related to the levels at which the colors are actually used under normal conditions.

Some of the ingredients used in testing FD&C Red #32 came from a source not identified and not shown to be pure or coming from a source where it was used in the manufacture of Red #32.

Based on what has been said heretofore, we respectfully object to the entry of an Order abandoning the use of FD&C Red #32 for the use of coloring oranges, and respectfully request that the Secretary either send the matter back for further testimony as to whether FD&C Red #32 is harmless in the manner and extent to which it is used, or that the Secretary modify her Order so as to allow FD&C Red #32 to be used on the outside of oranges for coloring.

The Supreme Court of the United States has held

[fol. 202] "The settled administrative construction of a statute by those instructed with the duty of enforcing it, is entitled to great weight." (U.S.A. vs. C.N.S. & M R.R. Co. 288, US 1, (77 Law Ed 583); Brewster vs Gage, 280 US 326, 74 Law Ed. 457.)

We respectfully submit that a department of the Government should apply the same regard for a long established construction on which formal hearings had been had before determining and had been recognized for more than a quarter of a century, and under which construction more than a quarter of a billion boxes of oranges (Over 256,000,000) (Exhibit 7) have been shipped, without a single complaint, and without any showing of any danger to any consumer.

We respectfully urge the continuation of the use of FD&C Red #32 on the outside of oranges for coloring.

Respectfully submitted, (S.) J. Hardin Peterson,
Attorney at Law, Attorney for Users of FD&C
Red #32 Named in detail in the original Brief
filed in this matter.

Lakeland, Florida.

[fol. 203] SUPPLEMENTAL A-1 TO BRIEF

Food Machinery and Chemical Corporation
Florida Division
Lakeland, Florida

March 16, 1954.

FD&C Red No. 32 in Color Added Oranges

Two separate laboratories, Food & Drug Administration and the Florida Citrus Commission, have run independent analyses on color added oranges and have found that they contain only 4 parts per million of FD&C Red No. 32 on the basis of the total weight of the fruit. An average orange weighs 200 grams (about 1/2 lb) and contains therefore about 0.0008 grams (8 ten thousandths) of FD&C Red No. 32, all of which is of course on or in the outer peel.

In Dr. Vos' testimony, shown as Exhibit No. 4 in the Hearing held January 19, 1954, a series of experimental feeding tests were reported.

On page 1, results are recorded covering an experiment conducted in 1940 in which rats were fed a daily diet containing 0.10% FD&C Red No. 32 over an extended period of time beginning with rats which were only 21-22 days old.

On a comparable basis, assuming that a man eats an average of 4 pounds of food per day, 0.1% Red No. 32 would amount to 0.004 lbs of color or 1.8 grams. One pound is equivalent to 453.6 grams. In order to eat 1.8 grams of color (on the basis of 0.0008 grams of color per orange) a man would have to eat 2250 oranges—peel and all each [fol. 204] day. This is approximately 1100 pounds of oranges that would have to be eaten per day and is approximately 7 times a man's weight.

Another comparison might be made by assuming that a man ate 6 oranges, peel and all, per day. On the basis that a color added orange contains 0.0008 grams of color, this would amount to 0.0048 grams. By comparison with the rat feeding level of 0.1% in the diet, and a man eating 4 lbs of food per day he would have to eat 1.812 grams of dye. $1.812 \div 0.0048 = 378$. Thus the rats were fed at a level of 378 times as much color as a man would get if he ate 6 oranges, peel inclusive, per day. This would amount to 1134 times as much, on the basis that a man ate two oranges per day.

On page 4 of the Exhibit is reported an experiment in which rats were fed at 2.0; 1.0; 0.5 and 0.25% levels. Since at the 0.1% level a man would have to eat 2250 oranges, then at these levels he would have to eat 45,000; 22,500; 11,250; and 5,625 respectively.

Assuming on the other hand that a man ate 6 oranges, peel included, per day, then on the basis of 0.0008 grams of color per orange, the total would be 0.0048 grams. On the basis of a man eating 4 lbs. of food per day, the 2.0% level would require 36.24 grams of dye. This amounts to $(36.24 \div 0.0048) = 7550$. Thus the rats were fed at the rate of 7550 times as much color as a man could get if he ate 6 oranges (peel inclusive) per day. At the 0.25% level this rate is 944.

[fol. 205] In the 1938-44 experiments reported on page 21, dogs were fed by means of capsules as much as 100 mgs

of color per kilogram of body weight per day. An average man weighs 70 kilograms (150 lbs) and therefore would consume 7000 mgs of color if fed at the same rate. Since a color added orange contains 0.8 mg of color it would take 8750 oranges for a man to get 7000 mgs of color per day. This is approximately 4380 pounds or about 29 times as much as the man weighs.

Again assuming that a man might eat 6 oranges (4.8 mg of color) per day then this represents that the dogs were fed at a level of $7000/4.8$ or 1458 times as great. Yet in this report in spite of the high level of feeding, it was reported that the dogs showed no ill effects except for moderate weight loss.

Subsequent to this the same dogs were fed at the rate of 20 mg per kilogram per day for a period of 5 years with no ill effects. This is $1/5$ the 100 mg level. On a comparable basis a man would have to eat 1750 oranges per day for the five year period. In this experiment the dogs were found to experience no ill effects.

In the 1952 experiment reported on page 29, dogs were fasted over night, then given 200 mg of color in a capsule, and then fed two hours later. It was reported that 8 of 10 dogs developed diarrhea. This, of course, is an unnatural way of feeding. Nevertheless, on this basis a man would have to eat 7 times or 1400 mg on a comparable basis and this would require 1750 oranges. This amounts to 875 pounds or more than 5 times the man's own weight. On the [fol. 206] basis of 6 oranges per day the dogs were fed at a level of 292 times as much as a man would get if he ate 6 oranges (peel inclusive) per day.

Dr. L. G. MacDowell, Director of Research for Florida Citrus Commission, testified that his laboratory's analysis of juice extracted commercially from color-added oranges showed that it contained 0.07 parts per million of Red No. 32. It should be pointed out that rarely, if ever, does a canning plant run 100% colored oranges. Generally the fruit is a mixture of grove-run and packing house elimination. It is true also that this trace of color gets into the juice in the course of the commercial extraction and is not in the juice prior to that operation.

It may be assumed that an individual might drink as much as 8 ozs. (approximately 250 grams) of juice per day. This represents only 0.0175 mg or 0.0000175 grams (453.6

grams per pound) of color. Assuming that a man eats 4 lbs (1800 grams) of total food per day this amount of color is 0.000001% of the total daily diet. Compared with those experiments in which Dr. Vos employed feeding levels of 0.1%, this represents 1/100,000 of his level or it might be said that his level was 100,000 times as much as a man might get by drinking 8 ozs of orange juice per day.

As stated earlier, Dr. Vos reported on page 21 and 22 of Exhibit #4 that in experiments conducted in 1938-1944 dogs were fed 20 mg of color per kilogram of body weight per day over a period of five years and no adverse effects were noted nor was there any accumulative effect.

[fol. 207] On a comparable basis a man weighing 70 kilograms would have to 70x20 or 1400 mg of dye per day. As shown above, 8 oz of orange juice might possibly contain as much as 0.0175 mg of dye. This then would represent (1400—0.0175) or about 80,000 such 8 oz drinks or 5000 gallons of juice per day. By analogy a person could drink a 5000 gallon tank full of orange juice every day without suffering any ill effects attributable to the presence of dye-stuff.

On the basis of a man drinking 8 ozs of juice per day containing 0.0175 mg of color, this is only 1/80,000 of the intake which caused 'no effect' when the dogs were fed for five years.

In view of the foregoing considerations, it is submitted that the feeding levels of this dye employed in the experiments reported by Dr. Vos are fantastically greater than the amounts or levels that a person might get by eating oranges or by drinking the juice. It is clearly evident from the testimony presented at the Hearing that no evidence was submitted to show that consumption of the infinitesimal amounts of dye which might be consumed by eating color-added orange or juice therefrom has any harmful effects whatsoever.

R. D. Gerwe, Research Department, FM&CC.

[fol. 208]

Copy

Mutual Orange Distributors, Redlands, California, U.S.A.

March 4, 1955.

Airmail

The Honorable Oveta Culp Hobby, Secretary of Department
of Health, Education and Welfare, Washington, D. C.

DEAR MADAM SECRETARY:

Re: Color Certification

Speaking for the approximately three thousand grower members of this cooperative marketing association of California and Arizona citrus producers, this letter is sent you to be certain that in the consideration of this general subject, you understand that if there is an available certified color, our members are extremely interested in its use on fruit which, principally because of growth changes, does not have an appearance attractive to customers even though its interior qualities are of the highest.

Yours sincerely, (S.) Robbins Russel, General
Manager.

RR:as

[fol 209] Before Department of Health, Education and
Welfare.

In the Matter of: Amending Par, 135-3 and 135.11 of the
Color Certification Regulations

Docket No. FDC 60

PETITION

Comes now Frank R. Schell, of 1602 Richardson Place, Tampa, Florida, and respectfully petitions that the proceedings in the above cited matter be reopened, for the purpose of offering additional testimony and other available evidence which will disclose that, in fact and in law, the Food Color FD&C Red No. 32 is harmless within the lawful

meaning of Section 406 (b) of the 1938 Food, Drugs and Cosmetics Act, and in support of said petition respectfully shows:

(1) The said Frank R. Schell has a financial interest in the successful use of the said process and is a grower of citrus fruits, but, and far more important, he has a direct and heavy responsibility to the Florida and Texas citrus industries, arising out of the fact that he was the originator and inventor in fact of the Color-Added process for enhancing the varietal color of ripe oranges by the addition of a certified food color to the peel thereof, which process is the real target in these proceedings of Food and Drug Administration (hereinafter, for brevity, called F&DA).

The successful use of the Color-Added process in the States of Florida and Texas, during the years, particularly, [fol 210] of 1934 through 1945, was undoubtedly responsible, in large part, for the unprecedented growth of the citrus industries of those States, as the result of vastly increased production from trees planted during those years, so that, if those States be now deprived of the use of said Color-Added process; as a result of the present unjustified and unjustifiable attack thereon by F&DA, then the last case of the citrus industries of Florida and Texas will be far worse than it would have been had the Color-Added process never been invented, since the successful marketing of the huge volumes of oranges now produced in those States will be impossible should the use of the Color-Added process be, in effect, prohibited as the result of the efforts of F&DA to outlaw the certified food colors without which that process cannot be operated.

(2) The said Frank R. Schell is the only still living proponent of the Color-Added process who was actively engaged in all phases of previous efforts of F&DA to outlaw the Color-Added process, during the years 1933-1938, and should have been heard in this important matter.

(3) The said Frank R. Schell had no notice that any proceedings to decertify the Food Color FD&C Red No. 32 and thereby destroy the Color-Added process, were under contemplation by F&DA, until the formal notice that hearings had been set for January 19, 1954, was published in the Federal Register of December 19, 1953. Even the meager information thus had was accompanied by assurance that

these proceedings were not directed at the Color-Added process, and by the time the said Frank R. Schell received [fol. 211] other and correct information, it was far too late to find, employ and inform counsel as to the complexities of the case and for such counsel, if found, to make any proper preparation for the hearing held on January 19, 1954. Therefore, the said Frank R. Schell was unable to be represented by counsel at such hearing and, as a result thereof, the record is incomplete as to many facts of the greatest importance which should constitute a part of the record in these proceedings.

Wherefore, the said Frank R. Schell now respectfully petitions the Secretary of the Department of Health, Education and Welfare to re-open the proceedings in this said Docket No. FDC-60 and to fix a date for rehearing thereon at which time all of the facts essential to a decision therein that will accord with law and justice may be made a part of this record, in fairness to those industries whose very existence is now threatened by the unlawful attack being made thereon by F&DA.

Denied.

The said Frank R. Schell further respectfully shows that, if this petition to reopen be granted he can and will show that the coloring medium (FD&C Red No. 32) affects only the oily and waxy outer surface of the peel (a layer of only about 1/1000 inch in thickness) of oranges colored therewith; that the color does not and cannot penetrate the white cellulose of the peel, or the "rag, or the pulp, or the juice, other than the minute quantity (7/100 of 1 part per million) of color carried in the oil which escapes into the juice during extraction; that such coloring matter is not and cannot be [fol. 212] dangerous to human health, or other than harmless thereto; that personnel working with said FD&C Red No. 32, in the manufacture of Color-Added materials furnished to packinghouses, and in servicing the process in packinghouses, have had their clothing, their hands and their skin above the waist-line soaked with the color during working hours for months at a time, have inhaled the fumes therefrom and have ingested the said color, without any adverse effect on their health; that the amounts fed to test animals, in relation to any amounts that could ever be con-

sumed by any human being, through eating Color Added oranges, or drinking the juice thereof, or eating any food in which such color has been used, have been so excessive as to be fantastic; that such unrealistic tests have no relationship to the question of whether or not such color is "harmless" within the meaning of the statute, hence are wholly irrelevant and immaterial to the issues in this cause and should be stricken from the record; and other pertinent matters which could, and would have been shown at the hearing had on January 19, 1954, save for the fact that proponents of the Color Added process had been induced to inaction by assurances had that these proceedings were not directed at that process, receiving no information, until January 1, 1954 (far too late to make any proper preparation for such hearings), that the complete destruction of the Color Added process constituted the real objective of Food and Drugs Administration in the institution of these proceedings.

Further reasons why this petition should be granted are contained in this petitioner's Exceptions to Order promulgated on December 29, 1954, and in petitioners Brief on [fol. 213] said Exceptions, the said Exceptions and Brief being hereto attached and by this reference made a part of this Petition as fully and completely as if herein set forth verbatim.

Your petitioner further respectfully prays, should this petition be denied by the Secretary of Health, Education and Welfare, that, as alternative relief, he be admitted as a party to these proceedings and that his Exceptions to the proposed order and to the Findings of Fact filed by F&DA in support of the effort to secure promulgation of such order, and the brief by Frank R. Schell in support of his said Exceptions, all hereto annexed, be now admitted to the record in these proceedings and given the same fair and conscientious consideration as is due them and the other briefs filed in connection with said subject matter.

Allowed.

(S.) Frank R. Schell.

Tampa, Florida, 1602 Richardson Place.

March 5, 1955.

[fol. 214] In the Matter of: Amending Par. 135.3 and 135.11
of the Color Certification Regulations

Docket No. FDC-60.

Exceptions to Order and Brief on Exceptions

FOREWORD

In explanation of what might otherwise be considered an unnecessary digression, we respectfully submit our conviction that an impartial appraisal of the issues involved in these proceedings cannot be properly approached without an appreciation and consideration of the history of prior efforts by Food and Drug Administration (hereinafter, for brevity, called F&DA) to outlaw and destroy the Color Added process, being a process for enhancing the varietal color of mature citrus fruits, particularly oranges, by the addition of an infinitesimal amount of a certified food color to the peel thereof.

We further respectfully submit our profound conviction that a careful evaluation of that prior history, together with a review of the record in the instant proceedings, will disclose that, beyond any reasonable doubt, these present proceedings constitute a renewal of similar efforts made by F&DA during the years 1933 to 1938, when, as now, the sole purpose thereof was to outlaw and destroy that process, the prior and present protestations of F&DA to the contrary notwithstanding.

[fol. 215] It is further respectfully submitted that consideration by the Honorable Secretary of the Department of Health, Education and Welfare, of the matters and things hereinafter recited, is not only right and proper, being a record of acts and things done by a subordinate Bureau of her Department, which can be verified by a careful inspection of the files of F&DA, but such consideration is required in the interest of truth and justice and of morality in Government.

It is further respectfully suggested that a review of those files may, perhaps, disclose the presently unknown and incomprehensible motive prompting this renewed attack upon the Color Added process, after more than 53 billions of oranges had been colored by the certified

food colors employed in that process, over a period of more than 14 years, without developing any slightest evidence, even yet, or eliciting the slightest complaint, that any person has ever suffered even a minor inconvenience, much less any injury or danger to their health, from eating Color Added oranges, or drinking juice from oranges colored thereby, although such juice has been a major item in the diet of, literally and actually, millions of babies.

It is further respectfully submitted that, very obviously, in these circumstances, the institution and prosecution of these proceedings by F&DA have not been grounded upon any possibility of injury to the public health, nor upon any necessity of protecting the public against fraud. Since the powers delegated to F&DA by the Congress are restricted to authority to prevent dangers to the public health and prevention of fraud, F&DA are, in this matter, acting without authority in law, and should be brought [fol. 216] back to a realization that F&DA, like all other agencies of Government, and all individuals, are bound by the law—not by their prejudiced conception of how the law should read—a fact which F&DA have ignored and flouted in these proceedings.

Nature and Early History of the Color Added Process

The Color Added process, in its simplest embodiment, comprehends a colloidal dispersion of a small amount of an appropriate oil-soluble, water-insoluble, certified food color, in an aqueous solution of soap and water, plus, in some instances, a small amount of solvent for the dye. The fruit is submerged in the coloring medium, or the coloring medium is sprayed on or poured over the fruit, for a period of several minutes, the coloring medium being maintained at a constant temperature of not to exceed 123°F.

The oil-soluble food color is absorbed by, or penetrates, *only* the very thin (about 1/1000 of an inch) layer of oily and waxy materials in the extreme outer covering of the peel. The oil-soluble color is chemically and physically incapable of coloring the white cellulosic material of the peel, or the white "rag" (membranes) of the interior, or the pulp, or the juice, being insoluble therein. An

infinitesimal amount of the oil-soluble color (about 7/100 of 1 part of color per million parts of juice, by weight) is sometimes carried into the juice in peel oil that escapes into the juice during extraction.

Conversely, the water-soluble, oil-insoluble colors are chemically and physically incapable of impregnating these [fol. 217] oily and waxy constituents of the peel with an added color, these waxy and oily materials being Nature's water-repellent safeguard against the fruit becoming water-soaked by rains, etc. But the water-soluble colors will color the white cellulosic constituents of the peel and, for that reason, a contrasting water-soluble color, usually green, is sometimes used in the Color Added process to mark breaks in the peel from clipper cuts, scratches, etc. enabling easy detection and elimination of such damaged fruits.

In the early months of 1933, the Color Added process was being readied for commercial use. Full information was given to Mr. Walter G. Campbell, then Chief of the Food and Drug Administration, a part of the Department of Agriculture, as to the materials in and use of the process, as above outlined. No objection by that Bureau had been anticipated, because the artificial coloration of mature citrus fruit had long been approved and promoted by the Department of Agriculture, which had determined and publicized the necessity for such artificial coloring practices, as witness the following excerpts from the official publications of that Department:

"Some of the early fall varieties of oranges and grapefruit ripen while the fruit is still green in color. Later varieties that mature in the spring or summer assume the color of full maturity during the winter while the fruit is still immature, but when warm spring weather occurs the rind may turn green again. Thus while the edible part of the fruit ripens, there is a 'regreening' of the rind. Grapefruit growing inside of densely foliated trees never develop full color, although some of the best-flavored fruit [fol. 218] is produced there. *There is, therefore, no definite relation between flavor or maturity and the color of the fruit while on the tree. However, there is a very significant relation between the color of the fruit offered for sale and the price that it will bring, and citrus fruit producers have*

always faced the problem of making the color of ripe fruit match its flavor." (Yearbook, U. S. D. A., 1932, pp. 134-137; emphasis ours.)

"It is well known that citrus fruits grown under certain climatic and cultural conditions may be mature and highly desirable for food while the skin of the fruit is still green in color. This is especially true of the Satsuma orange as grown in Alabama, where the fruit frequently reaches a state of physiological maturity at which it is palatable and attractive as an article of diet some weeks before it attains the characteristic golden yellow color. In general, when it reaches full color on the trees the fruit in this region is characterized by a low acidity, with a comparatively high sugar content, and the overripe fruit is inclined to be insipid in flavor. It is important then, if this fruit is to be furnished to the consuming public in its most desirable condition for food, that it be harvested before it becomes yellow on the trees.

"* * * On the other hand, green colored fruit, no matter what the quality, is difficult to merchandise. In the mind of the consuming public a green colored orange is immature and unfit for food. * * * The green colored fruit is therefore at a decided disadvantage in competitive selling. It is evident, then, that some method of treating this fruit so that it would assume a rich orange-yellow color early in the season, when it is most desirable for food, would be of [fol. 219] benefit to the industry and to the consuming public alike." (U. S. D. A. Bulletin 1159, August, 1923; emphasis ours.)

"The practice (artificial coloring of citrus) originated in California. It was first applied to the coloring of lemons and later adapted to oranges, particularly to Valencias, which have a tendency to become green late in the season, even though they have once assumed the golden-yellow color. Nearly all packing-houses are equipped with some facilities for coloring. At some seasons with certain kinds of fruit, it is a very common practice and considered one of the essential operations in preparing it for market. * * * (Parenthesis ours.)

"From a careful survey of the field, apparently there was no basis for the conclusion that the color of citrus fruit is an indication of its dessert quality or attractiveness as

an article of diet. * * * The color of the skin of the fruit when it has reached this stage in its development is partly a varietal characteristic and partly dependent upon the climatic and cultural conditions under which the fruit is grown. *It is obvious, then, that treating fruit which is physiologically mature or has reached a state in its development at which it has high dessert quality, so that it assumes a color or appearance pleasing to the eye and has a higher decorative value, is a legitimate practice in marketing and one which should be encouraged.*" (U. S. D. A. Bulletin 1367, May, 1926; emphasis ours.)

The ethylene gas process for "degreening" citrus fruit, then in universal use, had been invented and dedicated to the public by Dr. Frank E. Denny, of the Department of Agriculture, in 1923.

[fol. 220] The Color Added process had been necessitated by the fact that there is one variety of orange, produced in one competitive citrus growing area, which will attain an excellent but completely artificial color from the use of ethylene gas alone. While one of the orders of the Secretary of Agriculture, in the proceedings hereinafter recited, stated that the only effect of the ethylene gas process was to "unmask" the natural varietal color of the fruit, already present underneath the green, this statement was wholly incorrect. The color of that particular orange (produced in that one area) as disclosed when the green color first disappears, is the same pale, sickly-yellow found at that stage of processing on all other oranges produced in that area, and on all oranges produced in all other citrus producing areas. However, further exposure to ethylene gas, after all of the green coloration has disappeared, results in that particular orange attaining the rich orange-red color before mentioned, while additional exposure to the gas of all other varieties produced in that area, and of all oranges produced in other areas, results in no appreciable improvement in color.

As above stated, it was not anticipated that F&DA would or could have any possible objection to the use of the Color Added process, since it merely met the compelling necessity of citrus producers in all other areas to equalize the competitive advantage enjoyed by the producers and shippers of the orange which attained that most desirable

artificial color from ethylene gas alone. The Supreme Court of the United States had long before laid down the principle that it is the change in color, not the means employer, which is pertinent, even when that change constitutes but a removal of color.

[fol. 221] To our amazement, and consternation, Mr. Campbell promptly ruled that, if our process were permitted to be used at all, the oranges so colored, would have to bear a label, not on the wrappers and boxes alone, but on the peel of the orange itself, indicating the presence of the food colors used. That was bad enough, but, soon thereafter, Mr. Campbell advised us that any use of our process would be prohibited, whether or not the fruit was so labeled.

In May of 1933, this writer went to Washington and employed the firm of Palmer, Stellwagen and Scott to represent us in these proceedings before the Department of Agriculture, and to defeat the stated purpose and intent of Mr. Campbell to outlaw the Color Added process.

While, as above stated, it had never occurred to us that F&DA would show a preference for one method of artificially coloring citrus fruits over another process for accomplishing the same result, we soon discovered that F&DA and the producers of that one orange which attains an excellent artificial color from ethylene gas alone, were working closely together, as allies, to outlaw our process, which result would, of course, retain for those producers their prior monopoly of a satisfactory artificial color, with its almost unbeatable sales advantage. We did not blame those producers for trying to retain that advantage, any more than we would blame them if it develops that they are involved in this present attempt to destroy Color Added, which is quite possible. But we did censure F&DA then, as we would censure F&DA today, for improperly and secretly aiding either side in a competitive struggle wherewi-h no one in Government should be concerned.

[fol. 222] On October 31, 1933, our brief was filed. It was never answered, being unanswerable. On February 28, 1934, the Solicitor of the Department of Agriculture addressed to Secretary Wallace his opinion that the coloring of oranges by either the ethylene gas process or the Color Added process constituted adulteration, but further finding that, as to both processes, such adulteration could be cured

by appropriate labeling. In our case that meant stamping the words "Color Added" on the peel of the orange (that wording being used because it was not possible to make a die for use on small sizes which could carry the words "Artificially Colored" in the required type size) while fruit colored by ethylene gas alone would carry "Colored by Gas" or similar wording.

On March 9, 1934, in a letter to Mr. A. Mitchell Palmer, Secretary Wallace approvingly quoted this opinion of his Solicitor.

On July 16, 1934, after further argument and discussion, Mr. Wallace handed down his decision to the effect that oranges colored by the Color Added process must bear that labeling, but that oranges colored by the ethylene gas process would not have to be thus labeled, for the incorrect reason above recited.

It would seem that this should have put an end to the controversy, since this writer declined to institute Court proceedings challenging that order, the reason for so declining being that all early and late species of citrus fruit (not just oranges) in all citrus-producing areas are necessarily harvested with a green peel. It was realized that if we forced the issue in Court the result would, in all [fol. 223] probability, be the imposition of a label reading "Colored by Gas," or "Gas Treated," on all citrus fruits and, perhaps, other fruits such as bananas, apples, pears, etc., all of which are ethylene treated, since, under the law as above mentioned, it is the fact of a change in color, and not the means whereby that change is accomplished, which is pertinent and controlling.

We could not be sure that it would be at all possible to successfully market the large and increasing volume of citrus and other fruits with such labeling, and this writer would not risk injury to and, perhaps, the destruction of, the entire citrus industry and other fruit industries of the United States. Accordingly, from the first commercial use of our process, oranges so colored have borne the label "Color Added," while that particular orange, above mentioned, produced in that particular area, beautifully but artificially colored with ethylene gas alone, has gone unlabeled.

Mr. Cambell, however, did not abide by that order of Secretary Wallace, but continued his efforts to destroy the

Color Added process. There were further and continuing hearings before the Department of Agriculture in the fall of 1934, again in 1935, in 1936 and, finally, in 1937. Following this last hearing, Mr. Wallace, in about August of 1937, issued his final order, indefinitely postponing the effective date of an order outlawing the Color Added process, which order had issued on November 25, 1935, effective September 1, 1936, but had thereafter been postponed to become effective on September 1, 1937. With the issuance of that last order, Mr. Campbell ceased his attempts to persuade Mr. Wallace to go along with his fanatical prejudice against the use of any artificial color in or on any food.

[fol. 224] However, Mr. Campbell had not been relying upon only one string to his bow. While vigorously fighting the Color Added process, from early 1933 until August of 1937, in the Department of Agriculture, Mr. Campbell, ably and diligently assisted by Dr. Paul B. Dunbar, his principal assistant and successor in office, was fighting the Color Added process with every other weapon at his command. In 1935, he instigated the imposition of State embargoes against Color Added oranges by two States, and we barely escaped imposition of embargoes in a number of other States. We were able to fight off all of those embargoes because the State of Florida, at the first session of its Legislature after Color Added had gone into commercial use, had, at the instance of the Florida citrus industry and this writer, enacted its "Color Added Act," which imposed materially higher standards of maturity and quality for Color Added oranges than were required for oranges not so colored and very rigid State inspection to enforce these standards. (Those standards have been further raised, by later enactments, always at the instance of the Florida citrus industry, until, today, they constitute the highest standards of equality, not mere maturity, which any industry, producing any item of perishable fruits or vegetables, has ever imposed upon itself as to any such product, at any time, in any State.)

Again, there had been introduced in the Congress, in 1933, a proposed new Food, Drug and Cosmetics Act, which had powerful New Deal support. That 1933 bill carried language which would have empowered F&DA to outlaw

the Color Added process. Fortunately, however, it also carried other provisions which were so obnoxious as to [fol. 225] cause the proposed bill to be denounced by a number of Members of the Congress on the grounds that it would make F&DA the absolute dictator of the food, drug and cosmetic industries of the United States.

It must be recalled that there were not, in that Congress, very many Senators or Representatives who had not had forcefully called to their attention, by their constituents, cases in which legitimate business had been harassed by arbitrary and capricious acts of F&DA. Again, it should be further borne in mind that the Federal Courts had, on a number of occasions, rebuked F&DA for arbitrary and capricious actions and for attempts to expand its powers beyond those granted by the Congress.

In consequence of all of these things, that 1933 bill very fortunately failed of enactment.

Successive proposed Food, Drug and Cosmetics Acts were introduced in each session of the Congress, to and including the year 1937. While each succeeding proposed bill was a bit milder than the preceding bill, as to broader powers sought, each still contained provisions which could have been used by Mr. Campbell to destroy the Color Added process, and he and Dr. Dunbar contended mightily therefor.

That they were unsuccessful was largely due to the fact that, by such times, Mr. Campbell was well known to be an absolute fanatic on the subject of added artificial color in or on any food product—a fanaticism which has quite evidently persisted in F&DA to this day. For example, Mr. Campbell had attempted to procure the enactment, in the first of his proposed FD&C bills, of a repealer [fol. 226] of the Act of Congress of 1886 whereunder added artificial color is defined as a legal component of butter, which definition had been extended, by analogy, to cheese, no label declaration of the presence of such added color being required. This attempted repealer brought the dairy industry of the United States into opposition to Mr. Campbell's attempts to create for F&DA a dictatorship over the food, drug and cosmetics industries of the United States. In consequence, aroused representatives of affected industries were able to block enactment of all of these several proposed new bills.

The fanaticism of Mr. Campbell on this subject of artificial color in or on foods was well illustrated at a conference between that gentleman and our counsel, Messrs. A. Mitchell Palmer and Seiforde M. Stellwagen, at which conference this writer was present, which conference was held in about June of 1933. Mr. Campbell stated, very frankly, at the opening of the conference, that he was unalterably opposed to the use of any artificial color of any kind or character in or on any food product whatsoever, and, accordingly, was unalterably opposed to permitting the use of our Color Added process.

Mr. Palmer thereupon inquired whether that opposition would extend to the little vials of food colors which mothers buy to tint the icing on birthday cakes for their children. Mr. Campbell replied that the cake would taste just as good without any artificial color—a statement of doubtful authenticity, since it is well known that an article of food bearing an appealing color will be more appetizing than one without eye-appeal.

[fol. 227] Mr. Palmer then reminded Mr. Campbell that all of these colors were manufactured from base colors which Mr. Campbell's Bureau had certified as harmless and suitable for use in foods and that the use thereof had been recognized and approved for years. To this Mr. Campbell replied that whether or not the food colors were lawfully manufactured and sold was not the pertinent point; that the use of any food color in or on any food product was morally wrong and should be prohibited by law and that, if Mr. Campbell was successful in the efforts he then had under way, that result would ensue; that, for that reason, he was unalterably opposed to the Color Added process and did not intend to permit its use if at all possible to prevent the same.

The battle over the proposed new Food and Drug bills persisted until, in 1937, the bill known as S-5 (being the same number carried by the 1938 bill) was passed by both Houses of the Congress but, although the differences between the House and Senate bills were insignificant, still failed of final passage.

Thereafter, Mr. Campbell called on the Hon. J. Hardin Peterson, Representative from the First Florida Congressional District. He came, to use his own words, "with his

hat in his hand," stating that he knew when he was licked and had as well take his medicine gracefully; that if the Florida and Texas citrus people would cease their opposition to the passing of a new Food, Drug and Cosmetics Act, then, so far as he was concerned, those people could rewrite, to suit themselves, those parts of the proposed bill which they deemed inimical to the welfare of the citrus industry.

[fol. 228] Mr. Peterson telephoned that information to this writer on that same evening, and a delegation from the Florida citrus industry, including the writer, promptly went to Washington, there participating in conferences held by our attorney, Mr. Stellwagen (Mr. Palmer had died in 1936) with Mr. Campbell. Agreement having been had on necessary changes in language—and such agreement was readily reached—the others of the Florida delegation returned home, the writer remaining in Washington until the bill had been rewritten in final form.

There was a final (termed "buttoning-up") hearing by a Committee of either the House or the Senate, which was attended by Mr. Campbell, representatives of the dairy people, the drug industry, Mr. Stellwagen, this writer, and, as we recall it, some representatives of the cosmetics industry.

Because it was, as someone present termed it, "our last shot at the bear," the new bill was read and discussed almost paragraph by paragraph, requiring considerable time. Mr. Stellwagen, having a previous appointment, was forced to leave before the hearing was over, and asked this writer to remain and report to him on anything of importance thereafter transpiring.

We reached, finally, what is now Paragraph (b) of Section 406, regarding the certification of coal-tar food colors. Someone present—my recollection is that it was one of the drug people—inquired as to whether or not it would be advisable to define the word "harmless" as used in that sub-section. This writer immediately asked to be heard and stated that it was his understanding that all of [fol. 229] the prior decisions of the Courts interpreting, construing and applying the provisions of the 1906 Act, as amended, would be continued in full force and effect and be fully applicable in all future litigation under like pro-

visions of the new law; that the word "harmless" had been construed, over and over again, by those Courts hence, if these decisions were to continue in effect, there was no occasion for defining the word "harmless" in the new Act, but, if the new bill would have the effect of revoking those prior decisions, then that language should be enlarged to include that definition laid down by the Courts.

Mr. Campbell then took the floor, agreeing with the statement just made by this writer and stating that he was agreeable to such definition of the word "harmless" being inserted if desired, but that he, too, was under the distinct impression that the prior decisions of the Courts were to be preserved in full force and effect and would not be in any wise affected by the new law except where there was a specific repealer or other specific change that clearly voided a prior decision by the Courts on that particular point. Mr. Campbell went on to say, with considerable force and emphasis, that it was vitally important that the new bill should not affect that great mass of the law already embodied in prior decisions of the Courts; that, if those prior decisions were abrogated by the new act, it would then be necessary for his Department to re-establish, as precedents, each of the principles theretofore laid down by the Courts and that such an undertaking would require years of work and millions of dollars of unnecessary expense; that [fol. 230] he would have to request that his budget for F&DA enforcement services be at least tripled if F&DA was to be compelled to re-establish those old and controlling principles in every case that came up under the new law.

There was entire agreement among all present that those prior decisions of the Courts should not be disturbed by the new bill. The presiding officer then stated that he thought that it was clearly understood, and that it was certainly the understanding and intent of that Committee, as it would be the clear intent of the Congress, in enacting the new law, to retain and preserve in full force and effect the pertinent prior decisions of the Courts, making them fully applicable in future cases arising under like provisions of the new act. Accordingly, no definition of the word "harmless" was written into paragraph (b) of Section 406.

It is not the intent of this writer to say or imply that he has quoted the exact language used, but he does assert,

and would be only too happy to be sworn and to testify, that the foregoing is a fair and correct statement of what transpired in connection with that particular paragraph of the new law on that occasion.

It is Mr. Peterson's recollection that the minutes of the 1938 hearings were not printed, because prior hearings on the old bill S-5, which had failed of passage in the fall of 1937, had been voluminous, and it had been agreed that the record of hearings held on the old bill would be adopted as the record for the new bill. Most unfortunately, Mr. Peterson has been unable to locate the typewritten minutes [fol. 231] of any of the hearings on the new bill (some of which were more of the nature of informal conferences than formal hearings), including the minutes of this last "buttoning-up" hearing. However, should the Department of Health, Education and Welfare so desire, that record can be supplemented by sworn testimony, which is another reason why this writer's petition for re-opening this case, taking additional testimony and introducing additional evidence, should be granted. However, it is very likely that the foregoing statements will be completely substantiated by the records kept in Mr. Campbell's office at that time, F&DA having since cited and relied on those prior decisions.

Despite the fact that Mr. Campbell and Dr. Dunbar had fought the Color Added process vigorously, with every weapon they could lay hands on, from the early months of 1933 until agreement was had with the Florida and Texas citrus people on the provisions of the 1938 Act, it is to be noted that, once made, both Mr. Campbell and Dr. Dunbar kept their agreements religiously. There will be found in the files of F&DA a letter written by Mr. Campbell to one of the State enforcement officers, stating, in effect, that the matter of legitimacy of the Color Added process had been settled by Congressional action when the Congress enacted the 1938 Food, Drug and Cosmetics Act, in which it recognized the propriety of the Color Added process, and that, so long as the States of Florida and Texas policed their own industries and enforced the standards contained in State laws and the oranges carried the "Color Added" label, Mr. Campbell had no further interest in the Color Added process.

[fol. 232] Mr. Campbell gave similar assurance to a Florida citrus shipper at about that same time, but it is my recol-

lection that this last statement was made verbally, rather than in writing.

From that day in 1938—until sometime in the fall of 1952—something over fourteen years—by neither word or deed did F&DA ever indicate any opposition or enmity toward the Color Added process.

It is greatly to be regretted that the present officers of F&DA have seen fit to repudiate solemn agreements entered into by their predecessors in office and are now attempting, without rhyme or reason, much less authority in fact or in law, to bring about the abolition of that process, notwithstanding their admitted knowledge that the process cannot be dangerous to human health and that the continuing use of that process is imperatively required if the citrus industries of Florida and Texas are not to be destroyed.

That the present officials of F&DA have made this attempt gives rise to a question as to the real motive prompting their action.

We respectfully suggest and urge that the Department of Health, Education and Welfare institute a strict examination to determine that motive—that is, whether this attempt has been motivated by a flare-up of the old fanaticism against the use of artificial color in or on any food, or whether this is another attempt to increase the powers of F&DA to the point where it will have attained that dictatorship over the food, drug and cosmetics industry for which it contended so vigorously from 1933 into 1938.

[fol. 233] It hardly needs mentioning that, if F&DA can establish their interpretation of the word "harmless," as contended for in these proceedings—i. e., that no food color is harmless within the meaning of the law if F&DA pharmacologists can make any living creature ill by overfeeding and force feeding that animal with massive and fantastic amounts of the color, administered under unnatural conditions—then it is but one short step to applying that precedent and that interpretation to every other substance coming within the purview of the 1938 Food, Drug and Cosmetics Act, when that absolute dictatorship will have been attained.

The Secretary may find, of course, that these proceedings stem from a revival of the old alliance between F&DA and



other citrus interests, and that a corollary purpose of these proceedings may be to re-establish, for that old ally, its prior monopoly of a satisfactory artificial color for oranges, along with the above mentioned accruals to F&DA.

All of which, together with our Exceptions and Brief on Exceptions, which follow this Foreword, are

Respectfully submitted, Frank R. Schnell.

**EXCEPTIONS TO PROPOSED ORDER AND TO FINDINGS OF FACT
FILED BY FOOD AND DRUG ADMINISTRATION IN SUPPORT OF
SAID PROPOSAL.**

Exception No. 1: The Proposed Order is without authority in law.

Denied.

[fol. 234] Exception No. 2: The Proposed Order and the Findings of Fact filed in support thereof, are without foundation in fact.

Denied.

Exception No. 3: These proceedings were not initiated in good faith, nor have they been so conducted, by Food and Drug Administration.

Denied.

BRIEF

Exception No. 1: The Proposed Order is without authority in law.

Denied. See Conclusions 1-4.

This writer is no lawyer, hence is leaving the citation of cases and the like to the lawyers. However, having lived through twenty years of experience with Food and Drugs Administration, he is not uninformed as to the pertinent principles of law with which we are here concerned.

(a) The Proposed Order is not necessary for the protection of public health, hence the attempt to promulgate the same constitutes an attempt at usurpation of power by F&DA.

The Constitution of the United States reserves the general police powers over our people to the several States and, save for that reservation of powers in the several States, the Constitution, as written in 1787, would not have been adopted by the delegates to the Constitutional Convention, as is clear from the proceedings of the said Constitutional Convention, nor would it ever have been ratified by the original thirteen States. That reservation of powers has never been altered or repealed.

Therefore, the usages of such police powers as are enjoyed by the Federal Government, insofar as we are here concerned therewith, are strictly limited to such procedures and actions as may be required for protection against dangers to the public health (or against fraud upon consumers, with which latter clause we are not here concerned) arising out of the interstate transportation of articles of food, drugs and cosmetics, and such danger must be real and apparent, not wholly fanciful and imaginary, as is the nature of the alleged dangers inveighed against by F&DA in the instant case.

Whenever F&DA thus departs from that rule, it is the duty of the Department having supervisory powers thereover to bring its subordinate bureau back into line, with an appropriate reminder that we are living under a government of laws and not of men, from which laws F&DA are in no wise exempt.

As will hereinafter be shown, the real purpose and intent of F&DA, in these proceedings, is to outlaw the aforesaid Color-Added process. F&DA are, or should be, estopped from prosecuting such purposes and intent for the reason that in a letter to Hon. George A. Smathers, U. S. Senate, dated February 7, 1955, and signed by George P. Larrick, Commissioner of Food and Drugs, the following statement is made in the last paragraph of that letter:

[fol. 236] "The proposal to remove these coal-tar colors, including FD&C Red No. 32, from the list of colors eligible for certification for use in food results from the requirement of the Pure Food Law that only colors that are harmless are eligible for certification. Recently investigations show that these colors, when fed in *substantial* amounts, show evidences of toxicity. *There is, however, no evidence that, in the amounts used, and in the manner of use, in the*

coloring of citrus fruit, the product so colored is not safe for human consumption." (Emphasis ours. "Substantial" might well read "fantastic".)

(b) The Proposed Order is premised upon an attempted unconscionable interpretation by F&DA of the word "harmless" as used in Section 406 (b) of the 1938 Food, Drug and Cosmetic Act. As is clearly disclosed by the record of the hearing of January 19, 1954, it is the contention of F&DA that no color is "harmless," within the meaning of that Section of the Act, if F&DA pharmacologists can make any living creature ill by force-feeding massive and wholly fantastic doses of said color to such creature, under wholly unnatural conditions prescribed by F&DA's pharmacologists.

It is respectfully submitted that even pure water could not qualify for certification as "harmless" if such a weird construction of that word were permissible. It is a well settled fact of medical science that every living creature has a limit of tolerance for any and every substance that may be ingested by such creature and that if any substance be fed to any creature in excess amounts, then that creature will be made ill thereby, even though that substance be [fol. 237] pure water or pure proteins, which, taken in proper proportions, are the substances of like itself.

The contentions of F&DA in these records are contrary to all of the provisions of law governing the construction of language used in statutes since, without exception, it is required that the construction applied to a particular word in a particular statute must be a "reasonable construction" and in consonance with the purpose of the statute, which, in this case, is the protection of the public health, which F&DA, as above shown, have admitted is not and cannot be endangered by the consumption of the food color concerned through eating oranges colored therewith or drinking the juice from oranges so colored.

It is to be noted that a principal and most important use of F&DC Red No. 32 is its use for coloring oranges and that F&DA were formally advised, by representatives of the manufacturers, that they stand ready to restrict the use of that color to that purpose exclusively. F&DA has the power to so restrict its use and no objection would be entered to such restriction by proponents of the Color Added

process, although the record clearly discloses that consumption of the color, for any purpose, in any usual or customary amounts, could never be injurious to human health.

(c) The Courts have held, in many cases, that the "practical interpretation" or construction of doubtful or ambiguous language in a statute, which has been acted upon by the Department charged with its enforcement, will not be disturbed save for weighty reasons (See 280 U.S. 327). [fol. 238] From 1938 until 1952—14 years—the interpretation placed upon the word "harmless" by F&DA was that the substance concerned must be "harmless when consumed in the amounts and under the conditions of normal usage thereof" and F&DA have admitted that under that construction of the word "harmless", which F&DA gave thereto and consistently followed for all of those 14 years, the colors used in the Color Added process are completely harmless to human health. No weighty reasons—not even possible reasons—for upsetting that interpretation, at this late date, have been even suggested by F&DA, in these proceedings or elsewhere.

On the contrary, the complete absurdity of F&DA's contentions herein is illustrated and emphasized by the recent promulgation, by F&DA, of tables of tolerances for poisonous spray residues permitted to remain on fresh citrus fruit as sold to consumers. By those tolerance tables, F&DA permits such citrus fruits to bear 7 parts per million of arsenate of lead, a known deadly poison of known cumulative properties.

Thus F&DA is saying that the public health will not be endangered by eating oranges that carry, on the peel, seven parts per million of that known deadly poison, of known cumulative properties, but will be endangered by consuming oranges that carry, on the peel, four parts per million of a food color which it has certified, and for fourteen years permitted to remain certified, as being harmless and which the tests run from 1938 through into 1944, put in evidence by F&DA (and F&DA is bound thereby) conclusively demonstrate to be without either immediate or cumulative toxic properties.

[fol. 239] Where, then, are the "weighty reasons" required to support F&DA's fanciful theory, conceived just

14 years too late, that the Congress of the United States, by solemn enactment, authorized, and instructed, in Par. 406 (a) the fixing of tolerances for deadly poisons, then, in the very next paragraph of the same Section, forbade the use of any food color, however harmless under usual conditions of usage, if F&DA pharmacologists can make some living creature ill by force feeding that creature with huge and fantastic amounts of that color, ingested under unnatural conditions.

Those tolerances for poisons and the requirement for certification of food colors are contained in the same Section of the 1938 Act (406 (a) and 406 (b)). Certainly a strong argument can be made for (stronger than can be made against) the proposition that the provisions of Par. 406 (a) are applicable to the second paragraph of the same Section.

(d) Again, it is well known (being a fact whereof the Department of Health, Education and Welfare is charged with knowledge, since it is undoubtedly reflected by the files of F&DA for the year 1938) that the chief of F&DA, in Congressional Committee hearings on the 1938 Food, Drugs and Cosmetics Act, vehemently insisted that the great body of law contained in prior decisions of Courts of Competent jurisdiction, when interpreting the 1906 Act, as amended, must not be revoked or in anywise disturbed by the enactment of the 1938 Act, since, were those prior decisions negated by the new Act, years of time and heavy and unnecessary expense would be required to re-establish, as precedents, the principles laid down by those earlier [fol. 240] decisions of the Court. There being no dissent from any other person present at those hearings, the Chairman announced that everyone, including members of the Committee, were in entire accord on the point that it would be the intent of the Congress to preserve, in full force and effect, the prior decisions of the Courts, when interpreting the 1906 Act, as amended, making the same fully applicable when construing like provisions of the new Act.

It is unfortunate that the minutes of those hearings have apparently been lost, but this writer was present and heard Mr. Campbell's argument to that effect and the files of F&DA for 1938 will undoubtedly support these statements,

as will the records of subsequent cases prosecuted by F&DA, in which such prior decisions have been cited and relied upon by F&DA.

In numerous decisions, the Courts, interpreting the 1906 Act, held that before F&DA might interfere with the manufacture, transportation or sale of any properly labeled article of food or drugs transported, or offered for transportation, in interstate commerce, it must be shown that such article of food, or drugs, was injurious to human health when used or consumed in the amounts and under the conditions of normal and ordinary usage thereof.

F&DA are, therefore, in these proceedings, attempting to repudiate, not only their own construction of the word "harmless" which they had applied to that word for fourteen years, but are also attempting to repudiate their own insistence that the prior decisions of the Courts in interpreting the 1906 Act, as amended, should apply with like [fol. 241] force and effect to similar provisions of the 1938 Act, both of such attempts being contrary to law.

To Summarize: The Courts have said, plainly, on many occasions:

(1) That Constitutional limitations restrict the activities of F&DA to those necessary to protect against dangers to the public health and danger of fraud on the public, with neither of which dangers we are here concerned.

(2) That the language of a statute must be given a reasonable construction;

(3) That F&DA may not lawfully interfere with the manufacture, transportation or sale of any properly labeled substance contained in or on foods or drugs, absent a showing that the same is or could be injurious to human health when consumed in the amounts and under the conditions of ordinary and normal usage. Mr. Walter G. Campbell, Chief of F&DA, vehemently contended, in 1938, that the prior decisions of those Courts, construing the 1906 Act, must be preserved and made applicable in cases arising under like provisions of the 1938 Act;

(4) That the long continued interpretation or construction of doubtful or ambiguous language in a Statute, which construction has been acted upon by the Department charged with its enforcement, will not be disturbed save for weighty reasons. That construction for which this writer contends,

i.e., that the word "harmless" as used in the 1938 Act means [fol. 242] "harmless when consumed in the amounts and under the conditions of ordinary and normal usage", was first applied to that word by Mr. W. G. Campbell, Chief of F&DA, principal author and proponent of the 1938 Act, and by Dr. Dunbar, who was Mr. Campbell's principal assistant and successor in office. Certainly, Mr. Campbell and Dr. Dunbar were fully and completely informed and advised as to the intent of the Congress in its use of language, and, accordingly, of the proper interpretation and construction to be given this word "harmless" when used in connection with the certification of needed food colors. Yet, after fifteen years (1938-1953) of following such construction, without question, their successors now, without the required weighty reasons, or other excuse therefor, would reverse that construction, contrary to law.

Clearly, no justification can be found in law for the nonsensical statements of F&DA that they are compelled, by law, to contend that no food color is "harmless" within the meaning of the Statute if F&DA can make some living creature ill by force feeding that creature with fantastic dosages thereof, by means which constitute cruelty to animals.

Denied. See Findings 2-10.

Exception No. 2: The Proposed Order and the Findings of Fact filed in support thereof, are without foundation in fact.

We believe that, in view of the foregoing, it must be conceded that, for this proposed order to stand, it must be shown that the colors concerned are harmful to human [fol. 243] health, or offer a danger to human health, when consumed in the amounts and under the conditions of ordinary and normal usage, and that such danger must be present and real, and not some visionary or fanciful possibility, based on empirical experiments which bear no relation to reason.

It should be sufficient to invalidate the proposed order to cite the admission by Dr. Voss that no attempts have been made to relate the results of the experiments conducted on various animals to some showing of danger to human health and that F&DA have no information as to what

amounts of the colors would have to be ingested by a human being in order to be dangerous to human health—that, in other words, F&DA have no idea whether or not the evidence as contained in the testimony of Dr. Voss, and in the various exhibits, indicates a possible danger to human health. All they claim to know is that they can make an animal sick by feeding it that color, if they force enough of the color down its throat. All they claim is that such farcical experiments demonstrate that the color is not “harmless” under any and every imaginable circumstance, hence must be outlawed.

This is probably the first time in the history of American government when any government department has prayed for the issuance of an order which would clothe them with well nigh limitless powers, while admitting that they have no evidence that indicates whether or not the actions they would take thereunder are necessary in the public interest—yet that is exactly what F&DA are contending for in the instant case.

[fol. 244] It requires but a casual examination of the feeding tests conducted by the pharmacologists of F&DA to disclose that Dr. Voss could not have testified that such experiments disclosed a possible danger to human health. As admitted by F&DA in their presentment to the Secretary, when requesting hearings on this subject, the peel of a Color Added orange contains but 4 parts of the color per million parts of the whole orange. The uncontradicted testimony of the Chief Chemist of the Florida Citrus Commission, shows that the juice from Color Added oranges contains 710/0 of 1 part of the color per million parts of juice, by weight.

The test in which F&DA pharamacologists fed color to dogs at the rate of 5 milligrams of color per kilogram of body weight (at which level of feeding the dogs suffered no injury) comes closest to, but is yet far from being, an indication of the amount of color that could safely be ingested by a human being by eating Color Added oranges or drinking the juice thereof.

It is the accepted rule of pharmacology that such tests should be translated into an equivalent dosage for a man weighing 70 kilograms, or approximately 154 pounds, it being assumed that if the animal so fed is not injured thereby, then the human being would not be injured by an

equivalent dosage. Such an equivalent dosage for such a man (5 milligrams of color per 70 kilograms of body weight) would call for that human being to ingest 350 milligrams of color per day. To ingest that amount of the color by eating Color Added oranges, he would be compelled, according to F&DA figures, to eat 437.5 oranges per day, peel and all, [fol. 245] for the test period—extending, in some cases, over six years. For human being to ingest 350 milligrams of the color by drinking the juice from Color Added oranges, that human being would have to drink 1,250 gallons of juice per day for the test period.

The above, ridiculous as it is when offered in support of a contention that the color so used might be harmful to human health, is but mildly laughable when compared to other tests which F&DA would have us believe indicate a possible danger to human health from the consumption of such food colors.

In other tests, dogs were fed 20 milligrams of color per kilogram of body weight, which would be equivalent to a dosage of 1400 milligrams for that human being weighing 70 kilograms, or 154 pounds, and to ingest that 1400 milligrams of color from eating Color Added oranges, that human being would have to eat, every day of the test period, 1,750 Color Added oranges, peel and all. To ingest that amount of color from drinking the juice of Color Added oranges, that person would have to drink 5,000 gallons of orange juice each day for the test period.

Other animals were fed 100 milligrams of color per day. The equivalent human dosage would be 7,000 milligrams of the color per day, for that 154 pound human being. To ingest that amount of color from eating Color Added oranges, that person would have to eat 8,750 oranges per day, peel and all, or drink 25,000 gallons of juice per day, for the test period.

Such is the preposterous nature of the tests which F&DA [fol. 246] has had the temerity to ask the Department and, eventually, the Courts, to say are sufficient to warrant the destruction of the citrus industries of Texas and Florida, through decertification of these colors.

As further supporting the allegations of Exception No. 2, attention is respectfully directed to the following:

(1) Re Finding of Fact 2: It is asserted that: "Because of advances in knowledge and techniques in the field of

pharmacology, the Food & Drug Administration has initiated new tests to explore more fully the toxicity of the certifiable coal-tar food colors. This involves the application of all techniques and procedures now considered necessary to assure proper evaluation. A number of these tests, with present-day techniques and procedures, have been conducted by the Division of Pharmacology of the Food and Drug Administration, using FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32."

The reason for that language is quite clear—exhaustive tests to determine both the immediate and cumulative ("chronic" is the new—and incorrect—word) toxicity of the color FD&C Red No. 32 had been run, by F&DA, over a period of five to six years, the result of such tests being a finding that such color had no appreciable toxicity, immediate or cumulative. Some means had to be found to discredit those tests, as justification for this new attack on the Color Added process. So we have this quoted language, obviously designed to mislead the uninformed into believing that the tests run from 1938 into 1944 were unreliable in the light of "advances in knowledge and techniques in the field of pharmacology."

[fol. 247] The cold, unadorned facts are these:

(a) That if there have been such "advances in knowledge and techniques in the field of pharmacology", F&DA has not used such advanced techniques in any of the tests reflected by the Exhibits put in evidence by F&DA. There is no single step followed in the tests run in 1952 and 1953, as shown by those Exhibits, that were not known and followed by research workers prior to the 1938-1944 tests.

(b) That, far from discrediting the tests run from 1938 to 1944, the tests run in 1952 and 1953 are, instead, discredited by the prior tests, because these later tests were by no means as comprehensive as the 1938-1944 feeding tests, nor does the analysis of the results of these later tests even approach the excellence of the analytical work done following the 1938-1944 tests, either in scope or as to fundamentals.

(2) Throughout the Findings of Fact filed by F&DA, we find references to loss of weight, coupled with references to diarrhea induced by such feeding. But nowhere in the Exhibits is there any reference to an inevitable fact—that much of this weight loss was due to malnutrition, due to the animals refusing food containing excessive amounts of color.

Instead, we are left—and intentionally do—to believe that every adverse effect noted is directly attributable to the consumption of the food color concerned.

(3) There are several references, in the said Findings of Fact, of tests for cancer, but no mention, anywhere that the results of such tests were negative.

[fol. 248] (4) In tests of this kind, the content of the "basic diet", and the amount thereof fed to these animals is of vital importance in appraising the results of such tests. This information is not given in either the Exhibits or Findings of Fact.

(5) There are repeated uses of the word "normal" in the Exhibits forming the basis for tests reported in Findings of Fact, but nowhere is this word defined, nor is it possible of definition.

(6) Reference is made to unfinished experiments, a curious practice in proceedings where a basic agricultural industry of two great States is thereby threatened with possible destruction.

(7) At pp. 8 and 9 of the Exhibits, reference is made to the gross pathology of formalin fix tissues, which references are not entirely accurate, as, for example, the reference to "rough surface" of livers. The meaning and significance of the term is not stated. "Nutmeg livers" occur in many healthy animals. Parasites cause extensive damage to both livers and bile ducts.

The foregoing are a few of the many weaknesses and inaccuracies to be found in Exhibits and Findings of Fact which prompted and required this writer's petition for a reopening of these proceedings and the taking of full and complete evidence in the cause.

Obviously, in view of the prior decisions of our Courts that, before F&DA may prohibit the manufacture, transportation or sale of any properly labeled article of food [fol. 249] under an allegation that the same is or may be dangerous to health, it must be shown that such danger is real and apparent, not fanciful and imaginary, and that such article must be dangerous to human health in the amounts and under the conditions of ordinary and normal usage, each and every the contentions of F&DA must be overruled and the entire record of tests run, based on such travesties of alleged research as those hereinabove recited, must be held to be wholly meaningless and completely ir-

relevant insofar as concerns any relationship to human health, absent which relationship F&DA's attempted outlawing of these colors must be held to be an arbitrary and capricious abuse of delegated powers.

It is respectfully submitted that the Department of Health, Education and Welfare, which is charged with the duty and responsibility of policing the acts of its subordinate bureaus, may not lawfully uphold the fanciful contention of F&DA that the Congress of the United States solemnly enacted a statute which not only authorized, but instructed, that F&DA not only may, but must, outlaw any color, on the grounds that it is not "harmless", if the pharmacologists of F&DA can make any living creature ill by overfeeding and force feeding that creature with huge and fantastic quantities of such color under wholly unnatural conditions—as when a dog was fasted and then given 100 milligrams of the color, dissolved in oil and contained in a capsule, forced down the dog's throat, when its stomach was empty.

If that contention is not the ultimate in absurdity, certainly it is the penultimate, when it is considered that thus feeding pure proteins, or pure water, would likewise make [fol. 250] that animal ill, although those substances, when properly fed, are indispensable to life itself.

Exception No. 3: These proceedings were not initiated in good faith, nor have they been so conducted, by Food and Drug Administration.

Denied.

This writer fully appreciates the gravity of the allegations of this Exception but respectfully submits that, since it is clear on the record that there is no justification to be found, in law or facts, for the attempted outlawing of the Color Added process, by decertifying the food colors essential to the operation thereof, such allegations are not only proper but required, to the end that the Department of Health, Education and Welfare may take such action as may be necessary to prevent a recurrence of such capricious and arbitrary abuse of powers by one of its subordinate bureaus.

In further support of this Exception No. 3 we respectfully recite the following:

These proceedings constitute a renewal of attempts made by F&DA, in the years 1933-1938, to outlaw the Color Added process, and a faithless repudiation of agreements had with F&DA in 1938. The details of those attacks and of that agreement were heretofore recited in more detail.

We have already mentioned that the first word we had of the contemplated action related to the hearings already set for January 19, 1954, which data was accompanied by information as to assurances given by F&DA (but not to this writer) that F&DA appreciated the necessity of the Color Added process to the citrus industries of Florida and Texas and that the proceedings thus instituted were in nowise directed thereagainst.

Then, on January 1st, 1954, just 16 days before said hearing was to be had, and, of course, far too late to make any adequate preparation to defend the Color Added process against the "sneak attack" thus launched, there appeared in the Tampa (Fla.) Tribune, under the by-line of Frederick Othman, a Washington columnist, a semi-humorous account of his troubles with some artificially colored sweet potatoes, in which he directly quoted Mr. George P. Larrick, then Assistant Commissioner of Food and Drugs, as saying:

"Larrick said I'd pounced on him at the exact psychological moment. Even as he examined the stains remaining on my hands, he said the administration's chemists were worrying about the colors going into *and in particular onto foods*.

"On January 19, he said, the administration would open formal hearings *on the subject of whether orange color with coal tar dyes*.

"The trouble is, he said, that some oranges, particularly in Florida, are still green colored when fully ripe. Citizens in other parts of the land refuse to buy 'em that color, so the packers have been dyeing them to make them look as sweet as they actually are. This has been perfectly legal. Each orange has borne the stamp: Artificially colored.

[fol. 252] "Some of these dyes used on oranges and in certain cakes, candies and soda pops" said Larrick, "were approved 40 years ago as non-injurious. Our chemists got to thinking a while back that perhaps they should take

another look. So they have been experimenting with animals, mostly rats, feeding them quantities of the colors mixed in their foods. They're gone about one-third way down the list of chemicals so far." (Italics mine.)

I am reliably informed that Mr. Larrick was asked about this statement that the upcoming hearings on January 19th were directed specifically to the question of "whether orange growers would be allowed to continue tinting their fruits orange color with coal tar dyes"; that Mr. Larrick did not directly deny the question, but stated that one couldn't go around denying what columnists write.

Thereupon, this writer wrote to Mr. Othman, asking verification or withdrawal of the stated quotation by Mr. Larrick, to which Mr. Othman replied, on January 20, 1954, as follows:—

"DEAR MR. SCHELL:

"I appreciated the temperateness of your letter and I certainly can understand your feeling about the investigation, but I must report that my dispatch accurately quoted Mr. Larrick except for the fact that I leaned over backward in an attempt to be fair to the citrus industry.

"What Larrick actually said was that his chemists were worried in particular about the toxic effects upon rats of [fol. 253] three coal tar dyes used to color Florida oranges. The other dyes used in soft drinks, candies and cakes he had not considered so deleterious.

"Cordially yours, (Sgd.) Frederick C. Othman."

It would seem, from Mr. Othman's first paragraph, above, that Mr. Larrick's comments to him were not exactly partial to the citrus industries of Florida and Texas.

Please note that Mr. Larrick was concerned, particularly, with food colors going on to foods, and was, indeed, so particularly concerned as to the color on oranges that the hearing set for January 19th had as its principal, if not only, subject matter, the question of whether the Color Added process should be outlawed. Please note, also, the statement that the toxicity of some of the colors—and the context makes that reference applicable to the colors used in that process—had not been re-examined in 40 years. Compare that statement with the facts clear on the record that the

color FD&C Red No. 32 had been tested, only 8 years before, in a manner far more thorough, even exhaustive, than the tests just run in 1952-53; that both tests showed that, as Mr. Larrick now admits in his letter of February 7th, 1955, to Senator Smathers, the oranges colored by the Color Added process are entirely harmless for human consumption—then note that, despite this knowledge, all had by Mr. Larrick when he gave this interview to Mr. Othman, he was statedly concentrating his fire on the Color Added process. When these facts in the record are thus compared, an impartial judge cannot escape the profound conviction that Mr. Larrick's primary objective in these proceedings has been, from the very first, the destruction of the Color Added [fol. 254] process, his prior and subsequent protestations to the contrary notwithstanding, and that the allegation of a lack of good faith on the part of F&DA in the institution and prosecution thereof is well founded.

That conclusion is further supported and firmly established by the nature of the tests that were run to accomplish Mr. Larrick's purpose to destroy the Color Added process.

For example: Dr. Voss testified that the recheck on possible toxicity of coal tar food colors was prompted by a complaint that a child had been made ill by eating candy in which a water-soluble color, FD&C Orange No. 1, had been used at a rate that figures out 2500 parts of color per million parts of candy, by weight. (Oranges cannot be colored with FD&C Orange No. 1).

Such an isolated occurrence—and the record shows that to be the only complaint received on that or any other color—was undoubtedly the act of an ignorant person which could be—and doubtless was—corrected by administrative action. Would the fact that this writer is allergic to sulfa drugs, or that some other person had been given and overdoes thereof, be justification for banning the manufacture thereof? Surely, we are not being asked to accept, either as good law or common sense, the theory that if an article is possible of being misused then manufacture thereof must be prohibited.

We deem it significant that, despite the fact that the only complaint received by F&DA had to do with misuse of a [fol. 255] water-soluble color, Mr. Larrick said, according to Mr. Othman's letter, that he did not consider the colors

"used in soft drinks, candies and cakes" (i.e., the water-soluble colors) so deleterious.

Yet the veriest tyro knows that the water-soluble colors, if toxic at all, are far more dangerous than are the oil-soluble colors (which latter, only, are capable of coloring an orange).

These water-soluble colors are soluble in their entirety in the aqueous matter of every cell in the human body, comprising some 90% of the entire body weight, so that their capacity for evil, if toxic at all, is limitless.

The oil-soluble colors, on the other hand, are soluble only in the oleaginous constituents, the fatty matter, of the body, so that only a minute amount is absorbed—and it harmless to human health.

These facts, undoubtedly well known to Mr. Larrick, and his F&DA chemists, force us to doubt their good faith when they suggest, as they have done on several occasions, that the proponents of Color Added should "adapt" some of the water-soluble colors to the coloring of oranges.

There is a long list of certified food colors, both water-soluble and oil-soluble. It is extremely doubtful that there is a single food color on that list, whether water-soluble or oil-soluble, which would not make an animal ill if fed to such animal in the fantastic dosages used in testing FD&C Orange No. 2 and FD&C Red No. 32.

[fol. 256] Yet the record is significantly silent as to any recheck having been made of the toxicity of any of those food colors except FD&C Orange No. 1 (the water-soluble dye as to which the one lone complaint had been received) and the two oil-soluble colors that are indispensable to the operation of the Color Added process which Mr. Larrick identified as his primary target in his remarks to Mr. Othman.

Other factors which cannot but bring in question the good faith of F&DA in the institution and prosecution of these proceedings are:

(1) The misstatements and inaccuracies in the Findings of Fact filed in support of the proposed order, hereinbefore discussed.

(2) Statements made that the language of the statute compels the decertification of these colors, when, in fact,

Mr. Larrick's attempts are being made contrary to all law and good morals.

(3) The farcical nature, before discussed, of the tests run by F&DA pharmacologists, the very obvious purpose thereof being to prove that, if so misused, those colors will make an animal ill, not whether such colors pose a danger to human health when used under any imaginable amounts or conditions of normal usage.

(4) The reiteration of the incredibly distorted viewpoint that no color may remain on the certifiable list unless it be incapable of making any animal ill when fed in fantastic dosages under fantastic conditions—coupled with the assertion [fol. 257] that F&DA have no alternative to decertifying any color that will not meet a test under which even pure water could not qualify as being “harmless”—while at the same time giving a clean bill of health to oranges carrying a content of arsenate of lead that is 75% greater than the amount of harmless food color found in the peel of a Color Added orange.

(5) The querulous complaints of F&DA that the manufacturers are “dragging their feet” in the matter of formulation a less toxic color, while insisting upon moving Heaven and earth to establish a construction of the word “harmless” under which no food color could ever qualify for certification.

(6) The “weasel worded” sentence that ends Point (3) in the Statement of Fact, which language is clearly intended to be interpreted, by the uninformed, as a statement that a certain amount of experimental work with FD&C Orange No. 2 and FD&C Red No. 32 has been done on man, that adverse effects therefrom have been observed but not “definitely confirmed”.

The fact is, of course, that F&DA have done no experimental work whatever with these two colors, with any human being. Why was there not used the forthright language set forth in the last sentence of the letter to Senator Smathers, dated February 7th, hereinbefore quoted? Could it be that the language used in the Findings of Fact were intended to mislead the Circuit Court of Appeals, should this cause finally come before that Court?

[fol. 258] (7) That when faced with an imminent disaster to the economy of two great States, arising out of what even F&DA must admit is, at best, a highly technical, strained and dubious interpretation of the word "harmless", we hear not one word from F&DA suggesting (or agreeing to) clarification of the Statute in such manner as to permit the continued use of a process which F&DA admits is completely harmless to human health and the record shows to be essential to the continued existence of the citrus industries of those States.

This record of reasons for inability to rely upon the good faith of F&DA in these proceedings could be extended indefinitely, but it is respectfully submitted that the foregoing should suffice to convince any impartial person that the real objective of F&DA, in these proceedings, is the outlawing of the Color Added process, their protestations to the contrary notwithstanding, and that the allegations of Exception No. 3 are well founded and proven on the record.

Conclusion

It is respectfully submitted that the allegations of the three Exceptions are fully sustained on the record, as pointed out in the brief.

It is further respectfully submitted and urged that (a) these proceedings should be dismissed instant and those responsible therefor in F&DA should be disciplined for their irresponsible conduct in instituting the same, but if that be denied, then (b): These proceedings should be re-[fol. 259] opened so that the record may be made to reflect the true facts, to the end that justice and morality in Government may be served.

Respectfully submitted, Frank R. Schell.

Tampa, Florida, March 5, 1955.

Before Department of Health, Education And Welfare:

PETITION OF THE CERTIFIED COLOR INDUSTRY COMMITTEE TO REOPEN HEARINGS IN THE MATTER OF AMENDING SECTIONS FORMERLY NUMBERED §§ 135.1, 135.5 and 135.11 OF COLOR CERTIFICATION REGULATIONS.

1. Petitioner, The Certified Color Industry Committee, is a Committee representing a group of coal-tar color producers whose membership includes the producers of approximately 90% of the coal-tar color produced in the United States for use in food, drugs and cosmetics. Among such colors are the colors formerly listed (and herein referred to) as FD&C Orange No. 1, FD&C Orange No. 2 and FD&C Red No. 32.

2. By an order of the Secretary, dated November 10, 1955 (hereinafter sometimes called the Order) promulgated under Sections 406(b), 504, 604 and 701 of the Federal Food, Drug and Cosmetic Act, as amended (21 U.S.C. 301 et seq.), [fol. 260] and published at pages 8494 and 8495 of the Federal Register of November 16, 1955, § 135.3 of the Color Certification Regulations, which listed the coal-tar colors which the Secretary will certify as harmless and suitable for use in foods, drugs and cosmetics, was ordered to be amended so as to delete therefrom FD&C Orange No. 1, FD&C Orange No. 2 and FD&C Red No. 32. The Order, effective February 14, 1956, was made pursuant to Notice of Proposed Rule Making published at pages 9352 and 9353 of the Federal Register of December 30, 1954, and after public hearings held on January 19, 1954.

3. The Order contains findings to the effect that the internal administration to test animals of FD&C Orange No. 1, FD&C Orange No. 2 and FD&C Red No. 32, at various levels of administration, caused damage to the test animals.

4. The maximum extent to which each such color is used in foods under normal conditions of use as set forth in Exhibit A annexed hereto and made a part hereof, is substantially less than the lowest level of internal administration of such color found by the Order to have caused damage to test animals.

5. The coal-tar colors which are the subject of the Order have important functions in food, drugs and cosmetics and have been in use for many years. Their discontinuance would cause hardship to the American public and an important segment of American industry.

Wherefore, petitioner, The Certified Color Industry Com-[fol. 261] mittee, without prejudice to the exceptions heretofore taken by it to the Order, respectfully petitions the Secretary to reopen hearings in the matter of amending Sections formerly numbered 135.3, 135.5 and 135.11 of the Color Certification Regulations, to take evidence as to the quantities of coal-tar colors FD&C Orange No. 1, FD&C Orange No. 2 and FD&C Red No. 32 used under normal conditions of use and by order to prescribe tolerances for such coal-tar colors within which they shall be continued to be certified as harmless and suitable for use in foods, drugs and cosmetics.

January 27, 1956.

Respectfully submitted, The Certified Color Industry Committee, By Michael F. Markel.

EXHIBIT "A" TO PETITION

Use of Coal-Tar Colors FD&C Orange No. 1, FD&C Orange No. 2 and FD&C Red No. 32 in Finished Foods Under Normal Conditions of use.

Food	Color Content* (parts per million)			
	Orange 1 (weighted average)	Orange 1 (maximum)	Orange 2 (maximum)	Red 32 (maximum)
Cakes, Cookies	19	163	—	42
Pies	31	236	—	—
Bread	—	1	—	—
Cheese	—	—	60	15
(Processed, American, etc.)				
[fol. 262]				
Ice Cream	—	0.3	—	—
Frankfurters	—	—	—	—
Bologna	39	90	—	—
Spreads	—	—	—	—
Oranges—fresh whole fruit	—	—	—	7
Orange—fresh peel	—	—	—	34
Canned & Frozen Vegetables	—	5	—	—
Candy	31	300	—	—
Desserts & Puddings	27	291	—	—
Soft Drinks	—	10	—	—
Condiments, Soups	—	5	—	—
Pickles, Olives, Prepared Dishes				

* Experimental Data.

Before Food and Drug Administration, Department of Health, Education, and Welfare.

ORDER DENYING PETITION OF THE CERTIFIED COLOR INDUSTRY COMMITTEE TO REOPEN HEARING.—Dated February 20, 1956

In the Matter of: Amending Sections 135.3, 135.5 and 135.11 of the Color Certification Regulations.

Docket No. FDC-60

The petition of the Certified Color Industry Committee [fol.263] to reopen the hearing for the purpose of taking additional evidence as to the "maximum extent to which each such color is used in foods under normal conditions of use" is hereby denied, for the following reasons:

1. Petitioner states that it is prepared to prove the maximum extent to which FD&C Red No. 32, FD&C Orange No. 1 and FD&C Orange No. 2 are used in foods under normal conditions of use; and that these amounts are substantially less than the lowest level of internal administration that caused harm to test animals.

2. Aside from the fact that the petition to reopen fails to controvert finding 8 which states that no safe level of administration to dogs of the color FD&C Red No. 32 was definitely established, it also fails to take into account the fact that man may be much more susceptible to harm from these colors than animals, as adverted to in finding 4. The general evidence which petitioner desires to produce would not change the order, if admitted, as explained below:

(a) Extent of Use of the Colors

The information contained in "Exhibit A" to the petition to reopen includes a list of finished foods in which it is alleged the colors FD&C Red No. 32, FD&C Orange No. 1, and FD&C Orange No. 2 are used in the amounts illustrated. The information in "Exhibit A" is more detailed than that adverted to in finding 10 supporting the final order, but it obviously is incomplete and no explanation is offered as to the meaning of "weighted

averages." Finding 10 would still be true if petitioner's [fol. 264] additional evidence as to amounts used were accepted. The evidence would show only the amounts of the colors used "under normal conditions of use" in the foods listed. The amounts occurring in other products would still be left to speculation, and there would be no limit upon the amounts of the colors which could be used under "abnormal conditions of use."

Since the close of the hearing, the Food and Drug Administration has investigated an incident in which popcorn colored with FD&C Red No. 32 caused severe illness to 196 children and adults. While this incident is not a matter of record, it serves to emphasize the point that colors listed for certification and certified as harmless by the Food and Drug Administration may be used in any quantity desired by food processors as well as manufacturers of drugs and cosmetics. Analysis of the popcorn referred to showed that it contained between 3,000 and 9,800 parts per million of FD&C Red No. 32. This figure is quite substantially larger than any found in "Exhibit A" which purports to show amounts of the colors used "under normal conditions of use."

The petition also fails to list the amounts of each color used in drug and cosmetic items, despite the fact that testimony that hearing establishes that the colors are used for coloring drugs and cosmetics (R. 102-106; 108).

The problem which would be encountered in attempting to determine the normal amounts of these colors which might be incorporated in the diet can be illustrated from the record in relation to FD&C Red No. 32. The witness, [fol. 265] Robert C. Evans, whose testimony appears at pages 91 to 98, testified that FD&C Red No. 32 is the principal color used in coloring oranges. He introduced Exhibit 7 which shows the number of oranges shipped from Florida for a number of years up to and including the 1952-53 season. Louis Gardner MacDowell, whose testimony appears at pages 98 to 106 testified that the average amount of dye contained on whole oranges was approximately six parts per million. A box of oranges weighs approximately 90 pounds. If we take the figures for the 1948 to 1949 season appearing on page 5 of Exhibit 7, we find the weight of the oranges colored that year

is approximately one billion eight million pounds. Assuming these oranges contained six parts per million of FD&C Red No. 32 that gives us a figure of approximately 11,000 pounds of this color which was used for coloring oranges. From the record of the hearing, this is the principal use of this color, yet the certification figures of the Food and Drug Administration show that for the past ten years the amounts of FD&C Red No. 32 certified have averaged 40,000 pounds. This leaves 29,000 pounds unaccounted for by the color estimated to be on the skin of oranges. The petition does not indicate that petitioner is prepared to show where this large amount of FD&C Red No. 32 would be used.

(b) Lack of Restraint on Quantities Used

Even if it were assumed that the figures presented in "Exhibit A" are accurate and complete at the present time, there is no way to guarantee that larger amounts of the colors will not be used in the future. The Federal Food, Drug, and Cosmetic Act makes no provision [fol. 266] for certifying poisonous coal-tar colors and then limiting the amounts of such certified colors which may be used in an effort to restrict the usage to safe levels. No standard or criteria have been established by the Congress whereby the Secretary may tolerate small amounts of poisonous colors in food, drugs, or cosmetics. In fact, an order establishing tolerances for a color which the Congress has stated in Sections 406(b), 504, and 604 of the Federal Food, Drug, and Cosmetic Act must be "harmless" would be contradictory by its very terms. Moreover, the Federal Food, Drug, and Cosmetic Act does not establish a standard or guide by which the Secretary could select some products, and exclude others, in allowing use of small amounts of coal-tar colors which are toxic. The only method by which such a result could be reached would be arbitrarily to state that the color or colors would be limited to some foods, drugs, or cosmetics and not to others. And neither the record nor the offer or additional testimony would establish any basis for choosing those products in which the colors should be allowed, and those in which their use would be prohibited.

(c) Proof of Harmlessness

The record of the hearing does not contain adequate scientific data to provide a basis for determining at what levels of consumption the coal-tar colors FD&C Red No. 32, FD&C Orange No. 1, and FD&C Orange No. 2 may be safely used without injury to man. The pharmacological studies included in the record on the toxicity of these colors were designed to determine whether the colors could continue to be regarded as harmless, rather than to provide information on which a safe tolerance could [fols. 267-280] be set. The experiments show that the colors are not harmless. They do not provide sufficient data to establish exactly how toxic the materials are so that a tolerance could be fixed with confidence. The tests may be regarded as "unrealistic" only if their purpose is misunderstood. They were designed for the purpose of determining whether the colors under consideration could be regarded as harmless. They were the tests customarily employed by competent toxicologists for that purpose. So far as is known, there are no pharmacological or other data in existence which in any way contradicts the results of the Food and Drug Administration's studies shown in the record.

The fact that testimony may be available that no harmful or toxic reactions have been detected from the ingestion of the colors in quantities used would not be controlling. This Department's responsibility under the Federal Food, Drug, and Cosmetic Act is to certify only such coal-tar colors as are harmless, so that possible injury may be prevented.

Marion B. Folsom, Secretary of Health, Education,
and Welfare.

Dated: Feb. 20, 1956.

[fol. 281] BEFORE DEPARTMENT OF HEALTH, EDUCATION AND
WELFARE

Food and Drug Administration

FINAL ORDER OF THE SECRETARY OF HEALTH, EDUCATION AND
WELFARE—November 10, 1955

Title 21—Food and Drugs

Chapter I—Food and Drug Administration, Department of
Health, Education and Welfare

Part 135—Color Certification

Miscellaneous Amendments.

In the Matter of Amending §§ 135.3, 135.5 and 135.11 of
the Color Certification Regulations

Wednesday, November 16, 1955.

By virtue of the authority vested in the Secretary of Health, Education, and Welfare by the Federal Food, Drug, and Cosmetic Act (secs. 406 (b), 504, 604, 701; 52 Stat. 1049, 1052, 1055; 21 U. S. C. 346 (b), 354, 364, 371; 67 Stat. 18), upon the basis of substantial evidence received at the public hearing held pursuant to the notice published in the FEDERAL REGISTER on December 19, 1953 (18 F. R. 8600), and upon consideration of the exceptions filed to the proposed order published in the FEDERAL REGISTER on December 30, 1954 (19 F. R. 9352), which exceptions were allowed or not allowed as appears from notations on the exceptions on file with the Hearing Clerk, Department of Health, Education, and Welfare, Room 5440, Health, Education, and Welfare Building, 330 Independence Avenue SW., Washington 25, D. C., the following order is hereby promulgated.

*Findings of Fact.*¹ 1. after a hearing in 1939 concerning

¹ The citations following each finding of fact refer to the pages of the transcript of the testimony and the exhibits received in evidence at the hearing, except for citations to the FEDERAL REGISTER, where applicable.

regulations for the certification of coal-tar colors, the coal-tar color now listed as FD&C Orange No. 1 (monosodium salt of 4-*p*-sulfophenylazo-1-naphthol) and the coal-tar color now listed as FD&C Orange No. 2 (1-*o*-tolylazo-2-naphthol) were found to be harmless and suitable for use in food, drugs, and cosmetics. After another hearing in 1939, concerning amendment of the coal-tar color regulations, the coal-tar color now listed as FD&C Red No. 32 (1-xylylazo-2-naphthol) was found to be harmless and suitable for use in food, drugs, and cosmetics. Accordingly, these three colors, among others, were listed with appropriate specifications of identity and quality in the coal-tar color regulations (21 C.F.R. 135.3) as certifiable for unrestricted use in foods, drugs, and cosmetics. (4 F. R. 1922, 1926, 1937, 3931, 3936, 3937; R. 46.)

2. Since that time the Food and Drug Administration has completed additional tests to explore more fully the toxicity of the certifiable coal-tar colors. A number of additional tests have been conducted by the Division of Pharmacology of the Food and Drug Administration, using FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32.

Tests that have been terminated are:

a. FD&C Orange No. 1:

i. Chronic feeding tests with rats on diets containing 0.1, 0.5, 1, and 2 percent.

ii. Chronic oral administration to dogs at doses of 5 milligrams per kilogram of body weight and 100 milligrams per kilogram of body weight.

iii. Cathartic tests in dogs, using single oral dose.

b. FD&C Orange No. 2:

i. Chronic or subacute feeding tests with rats on diets containing 0.01, 0.05, 0.1, 0.2, and 0.25 percent.

ii. Tests designed to determine carcinogenicity in rats, using weekly subcutaneous injections of approximately 5 milligrams. The test was inconclusive as to carcinogenicity and was discontinued after 8 injections. Three of the 18 test rats died on the dosage administered as compared to no deaths among the control rats.

iii. Carcinogenicity tests in mice, using subcutaneous implantation of 12.1 milligrams at intervals for 30 to 55 weeks. These tests produced no positive results.

iv. Chronic oral administration to 2 dogs at doses beginning at 100 milligrams per kilogram of body weight per day. The dosage was reduced successively to 20 milligrams and 5 milligrams in 1 dog, and to 20 milligrams in the other dog.

v. Chronic feeding tests in dogs at dietary levels of 0.2 percent and 0.04 percent.

vi. Cathartic tests in dogs, using single oral dose.

c. FD&C Red No. 32:

i. Chronic feeding tests with rats, on diets containing 0.1 percent.

ii. Subacute feeding tests with rats, on diets containing 0.25, 0.5, 1, and 2 percent.

iii. Chronic feeding tests with rats, on diets containing 0.1 percent and 0.25 percent.

iv. Carcinogenicity tests in rats, using weekly subcutaneous injections of approximately 5 milligrams to 10 milligrams. These tests were inconclusive as to carcinogenicity and were discontinued after 8 injections because 7 of the 18 test rats died or were sacrificed in extremis prior to the ninth injection. Similar toxic reactions were not encountered in the control rats. A second experiment, using weekly subcutaneous injections of approximately 1 milligram was also discontinued after 8 injections, because of deaths among the 18 test rats receiving FD&C Orange No. 2 in another part of this experiment.

v. Carcinogenicity tests in mice, using subcutaneous implantation of 10.8 milligrams at intervals for 35 weeks to 47 weeks showed no evidence of tumors.

vi. Chronic oral administration to dogs at doses of 5, 20, and 100 milligrams per kilogram of body weight per day.

vii. Chronic feeding tests in dogs at dietary levels of 0.04 percent and 0.2 percent.

viii. Cathartic tests in dogs, using single oral dose.

Tests of the three colors by external application to determine whether they are toxic when applied externally were being set up at the time of the hearing. (R. 8-78; Ex. 2, 3, 4.)

3. The tests with FD&C Orange No. 1 show that when taken internally at various levels of administration this color causes definite damage to various vital organs of the test animals, significant changes in body weight, and premature death.

This color caused the premature death of all rats on diets containing 2.0 percent of the test substance. Rats on a diet containing 1.0 percent of this substance showed marked retardation of growth, increased mortality, and chronic congestion and enlargement of the spleen. These same manifestations, to a lesser extent, were encountered in rats consuming a diet containing 0.5 percent of FD&C Orange No. 1. Dogs consuming 100 milligrams per kilogram of body weight per day of FD&C Orange No. 1 died in 26 months and 33 months. They had occasional diarrhea while alive and manifested terminal weight loss. Autopsy revealed congestion and atrophy of the liver attributable to the color. On a diet containing 1.0 percent of FD&C Orange No. 1, dogs exhibited chronic diarrhea. Rapid deterioration, and weight loss also occurred in 2 dogs. Autopsy revealed muscular dystrophic changes and testicular, prostatic, and uterine atrophy. These same manifestations occurred to a lesser extent in dogs on a diet containing 0.2 percent of FD&C Orange No. 1. A single dose of 100 milligrams to 200 milligrams of FD&C Orange No. 1 produced diarrhea in most dogs. Human volunteers who ate candy containing 0.07 per cent of FD&C Orange No. 1 exhibited diarrhea upon the ingestion of from one to eight pieces of the candy. Human volunteers taking 80 milligrams to 100 milligrams of the color in a single dose also experienced marked griping and diarrhea. (R. 14-22, 43-44; Ex. 2.)

4. Tests on rats at a level of 0.1 percent of the diet and on dogs at doses of 5 milligrams per kilogram of body weight per day did not produce any toxic effects attributable to FD&C Orange No. 1. However, these results must be contrasted with the diarrhea that resulted when human volunteers ate from one to eight pieces of candy containing 0.07 percent of FD&C Orange No. 1. This is particularly significant because man is shown to be more susceptible to the toxic effects of the color than are the test animals, and because the dogs having diarrhea (the symptom ob-

served also in man) showed damage to various vital organs after the chronic feeding tests. (R. 14, 16-18, 20-21, 43-44; Ex. 2.)

5. The tests with FD&C Orange No. 2 show that when taken internally at various levels of administration this color causes definite damage to various vital organs of the test animals, significant changes in body weight, and premature death.

FD&C Orange No. 2 caused severe growth retardation and increased mortality to rats on a diet containing 0.25 percent of the test substance. At 0.2 percent of the rats' diet, increased mortality and degeneration of the liver occurred. At a level of 0.1 percent of this substance in the diet, the rats exhibited marked growth retardation. At a level of 0.05 percent, autopsy revealed enlargement of the right side of the heart and, on microscopic examination, slight hypertrophy or hyperplasia of the cells in the liver. Approximately 5 milligrams per week given to rats by subcutaneous injection caused increased mortality and moderate growth retardation. Dogs consuming 100 milligrams per kilogram of body weight per day of FD&C Orange No. 2 lost weight or gained poorly. Twenty milligrams per kilogram of body weight per day caused one dog in the experiment to gain weight poorly. Five milligrams per kilogram of body weight per day apparently was tolerated by one dog without resultant injury. Dogs on a diet containing 0.2 percent of the test substance had diarrhea at the beginning of the experiment and exhibited [fol. 282] rapid deterioration and weight loss. Autopsy revealed atrophy of various vital organs caused by the color. At 0.04 percent of the diet, dogs gradually deteriorated and lost weight, and autopsy revealed atrophy of various vital organs. A single dose of 200 milligrams produced diarrhea in dogs. (R. 22-30; Ex. 3.)

6. FD&C Orange No. 2 caused damage to test animals at levels even lower than those at which damage was observed from FD&C Orange No. 1. The lowest level at which demonstrable harm to test animals was observed from FD&C Orange No. 2 was 0.04 percent of the diet of dogs. The lowest level at which FD&C Orange No. 1 caused demonstrable damage was 0.2 percent in the diet of dogs and 0.07 per cent when ingested by man in a single dose. (R. 18-19, 20-21, 28, 43-44, 67-68; Ex. 2, 3.)

7. The tests with FD&C Red No. 32 show that when taken internally at various levels of administration this color caused definite damage to various vital organs of the test animals, significant changes in body weight, and premature death.

When this color was fed to rats at a level of 2.0 percent of the diet, all the rats died within a week. At a 1.0 percent level, death occurred within 12 days. At 0.5 percent most of the rats died within 26 days. At 0.25 percent approximately half of the rats died within 3 months. All of the rats at this level showed marked growth retardation and anemia. Autopsy revealed moderate to marked liver damage. Similar but less severe results were obtained with rats on a diet containing 0.1 percent of FD&C Red No. 32. In addition to liver damage, however, autopsy also revealed enlargement of the right side of the heart in this latter group. Subcutaneous injection of approximately 10 milligrams per week caused death within 8 weeks to nearly half of the rats on the experiment. These rats exhibited anemia, hemorrhage and reduction in the size of the liver. Dogs taking 100 milligrams per kilogram of body weight per day showed moderate weight loss. A level of 0.2 percent of FD&C Red No. 32 in the diet of dogs caused rapid deterioration and weight loss and sporadic diarrhea; 0.04 per cent caused gradual deterioration and weight loss, sporadic diarrhea, moderate atrophy of vital organs, and muscular dystrophic changes; 0.01 percent in the diet caused weight loss and the death of one out of 4 dogs. A single oral dose of 100 milligrams or 200 milligrams caused diarrhea in the majority of the dogs tested. (R. 30-38; Ex. 4.)

8. The lowest level at which FD&C Red No. 32 showed damage to test animals was at 0.01 per cent of the diet of dogs. This was the lowest level at which the color was administered in the diet and, based upon the conversion figures appearing in the record, it is a lower dosage than the level of 5 milligrams per kilogram which produced no apparent effect on other dogs. Thus, no safe level of administration to dogs was definitely established. (R. 35-37, 40-42; Ex. 4).

9. The only known episode of illness in man was caused by FD&C Orange No. 1. It is the least toxic of the three

colors. The fact that no human ailment has been attributed to the other colors means little, because few people know what colors they are eating and the delayed toxic effects of the colors, as evidenced by the test animals, involve damage to vital organs and processes that would not have been attributed to the colors even if caused by them.

10. There was no evidence on which findings could be made concerning how much of the three colors is likely to be ingested by man from his food, drugs and cosmetics. Some interested persons, taking their own products, attempted to show that the amounts ingested would be small to the point of insignificance. But those contentions leave aside the occurrence of the colors in the products of others, as well as the fact that upon certification of a color the Department has no means of controlling the amounts of colors used in a variety of food, drugs, and cosmetics. Nor is there authority to limit a color, once certified, to a single food—for example, FD&C Red No. 32 for use in color-added oranges. (R. 20-21, 67-68, 98-108; Ex. 8.)

11. The coal-tar colors listed in the regulations as FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32 may be used at present in externally applied drugs and cosmetics as well as in products for internal consumption. Tests designed to examine the toxicity of these colors, when used externally, are not complete. (R. 46-48, 63-65.)

12. Modification of the coal-tar color certification regulations (21 CFR 135.11 (d) (2)) to eliminate the requirement for 3 months' written notice of change in composition of a coal-tar color mixture will facilitate the marketing of substitute mixtures and reduce confusion that may result from the deletion of a straight color from the listings at 21 CFR 135.3, 135.4, and 135.5. (R. 88, 89.)

Conclusions. 1. Based upon the above findings, the coal-tar colors FD&C Orange No. 1 (monosodium salt of 4-*p*-sulfophenylazo-1-naphthol), FD&C Orange No. 2 (1-*o*-tolylazo-2-naphthol) and FD&C Red No. 32 (1-xylylazo-2-naphthol), described in the coal-tar regulations (21 CFR 135.3) are not harmless and suitable for use in coloring food or for use in coloring drugs or cosmetics intended for other than external application.

2. Sections 406 (b), 504, and 604 of the Federal Food,

Drug, and Cosmetic Act (21 U. S. C. 346 (b), 354, and 364) provide for the listing of coal-tar colors that are harmless and suitable for use in food, drugs, and cosmetics. The act does not provide any method for listing toxic colors for specific food, drug, or cosmetic uses so as to limit their total use to small enough amounts that the toxicity might be disregarded. Under the statute a toxic color cannot be classified as a harmless color.

3. While a safe level of administration to test animals is disclosed by the record in the case of FD&C Orange No. 1, the record also discloses that that color has adverse effects upon man at a level well below the safe level of administration to test animals. The safe level of administration of FD&C Orange No. 2 to test animals is well below the level at which FD&C Orange No. 1 was found safe to test animals. It is, therefore, even more toxic than FD&C Orange No. 1. No safe level of administration was found even in test animals for FD&C Red No. 32.

4. The coal-tar colors FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32 are not harmless and suitable for use within the meaning of sections 406 (b), 504, and 604 of the Federal Food, Drug, and Cosmetic Act in coloring food or in coloring drugs or cosmetics intended for other than external application.

5. The coal-tar colors FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32 should be deleted from the listing at 21 CFR 135.3, since the Secretary cannot continue to list these colors as colors that the Food and Drug Administration will certify as harmless and suitable for unrestricted use in coloring food or in coloring drugs and cosmetics intended for other than external application.

6. Colors conforming to the present regulations and specifications for FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32 should be added to the listing at 21 CFR 135.5, for use in coloring externally applied drugs and cosmetics only.

7. The provisions of 21 CFR 135.11 (d) (2) requiring 3 months' written notice of a change in the composition of a coal-tar color mixture should be waived when such change is made necessary by deletion of one or more straight colors from the listings at 21 CFR 135.3, 135.4, or 135.5.

Therefore, it is ordered, That Part 135—Color Certification, be amended in the following respects:

1. In § 135.3 (a), delete the colors FD&C Orange No. 1, FD&C Orange No. 2, and FD&C Red No. 32.
2. Add the following to § 135.5 (a):

Ext D&C Orange No. 3

Specifications

Monosodium salt of 4-*p*-sulfophenylazo-1-naphthol.

Volatile matter (at 135° C.), not more than 10.0 percent.

Water-insoluble matter, not more than 0.3 percent.

Ether extracts, not more than 0.2 percent.

α -Naphthol, not more than 0.1 percent.

Chlorides and sulfates of sodium, not more than 4.0 percent.

Mixed oxides, not more than 1.0 percent.

Orange II, not more than 5.0 percent.

Pure dye (as determined by titration with titanium trichloride), not less than 85.0 percent.

Ext D&C Orange No. 4

Specifications

1-*o*-Tolylazo-2-naphthol.

Volatile matter (at 100° C.), not more than 0.5 percent.

sulfated ash, not more than 0.3 percent.

Water-soluble matter, not more than 0.3 percent.

Matter insoluble in carbon tetrachloride, not more than 0.5 percent.

o-Toluidine, not more than 0.05 percent.

β -Naphthol, not more than 0.05 percent.

Pure dye (as determined by titration with titanium trichloride), not less than 98.0 percent.

Melting point, not less than 128.0° C.

[fol. 283]

Wednesday, November 16, 1955.

EXT. D&C RED No. 14

Specifications

1—Zylylazo-2-naphthol.

Volatile matter (at 100° C.), not more than 0.5 percent.

Sulfated ash, not more than 0.3 percent.

Water-soluble matter, not more than 0.3 percent.

Matter insoluble in carbon tetrachloride, not more than 0.5 percent.

Xylidene, not more than 0.1 percent.

6-Naphthol, not more than 0.05 percent.

m-Xylidine in xylidine obtained by reduction of the dye not more than 30.0 percent.

Pure dye (as determined by titration with titanium trichloride), not less than 97.0 percent.

Boiling range of xylidine, obtained by reduction of the dye, 95 percent between 212°-232° C.

3. Amend § 135.11 (d) (2) so that, as amended, it will read as follows:

§ 135.11 *Labeling.* . . .

(d) . . .

(2) The name of such mixture is the same as or simulates the name of a previously certified batch of a mixture containing a different substance, or a different percentage of a pure dye; but this provision shall not apply if:

(i) The person who requests certification of such batch is the owner of such name and has given 3 months' written notice to the Food and Drug Administration specifying the change to be made in the composition of such mixture; or

(ii) Such change results from removal of a color from the listings in §§ 135.3, 135.4, and 135.5. .

Effective date. This order shall be effective 90 days after publication in the Federal Register.

(Sec. 701, 52 Stat. 1055; 21 U. S. C. 371)

Dated: November 10, 1955.

M. B. Folsom, Secretary. (Seal.)

[F. R. Doc. 55-9209; Filed, Nov. 15, 1955; 8:49 a. m.]

[fol. 284] MINUTE ENTRY OF ARGUMENT AND SUBMISSION
IN CASE No. 15934—May 8, 1957

(Omitted in Printing)

[fol. 285] MINUTE ENTRY OF ARGUMENT AND SUBMISSION
IN CASE No. 15948—May 8, 1957

(Omitted in Printing)

[fol. 286] IN THE UNITED STATES COURT OF APPEALS FOR
THE FIFTH CIRCUIT

No. 15934

FLORIDA CITRUS EXCHANGE, et al., Appellants,

versus

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare, Appellee

No. 15948

FRANK R. SCHELL, Appellant,

versus

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare, Appellee

On Petitions for Review of an Order of the Secretary of
Health, Education and Welfare

Before Hutcheson, Chief Judge, and Jones and Brown,
Circuit Judges

OPINION—July 12, 1957

JONES, Circuit Judge: In the nineteen-thirties growers
and packers of oranges in Florida and Texas began the
[fol. 287] practice of adding color to the rind of oranges.
Early oranges, maturing during warm weather, will ripen

to full maturity with the skin still green in color. Oranges maturing in the late winter or spring may fully ripen and undergo a "regreening" of the rind. The orange-purchasing public requires an orange-colored orange and will not accept those with green rinds. Representatives of a substantial number of those engaged in the growing and marketing of citrus fruits in the two states assert that severe economic reverses would result from a prohibition of adding color to the fruit; indeed it has been asserted that the future of the orange industry of these states is dependent upon the continued coloring of its product.

In 1938 the Congress enacted the present Federal Food, Drug and Cosmetic Act. 52 Stat. 1040; 21 U.S.C.A. §§ 301-392. The adulteration of food in interstate commerce and the introduction of adulterated food into interstate commerce were prohibited. 21 U.S.C.A. § 331. Congressional standards for determining when food would be deemed adulterated were set up.¹ Provisions for tolerances of poi-

¹ "A food shall be deemed to be adulterated—

"(a) (1) If it bears or contains any poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health; or (2) if it bears or contains any added poisonous or added deleterious substance which is unsafe within the meaning of Section 406; or (3) if it consists in whole or in part of any filthy, putrid, or decomposed substance, or if it is otherwise unfit for food; or (4) if it has been prepared, packed, or held under unsanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health; or (5) if it is, in whole or in part, the product of a diseased animal or of an animal which has died otherwise than by slaughter; or (6) if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health.

"(b) (1) If any valuable constituent has been in whole or in part omitted or abstracted therefrom; or (2) if any substance has been substituted wholly or in part therefor;

[fol. 288] sonous and deleterious substances were included.²

The Secretary of Agriculture, to whom the administration of the Act was originally committed, issued regulations on May 4, 1939, effective May 9, 1939, governing the

or (3) if damage or inferiority has been concealed in any manner; or (4) if any substance has been added thereto or mixed or packed therewith so as to increase its bulk or weight, or reduce its quality or strength, or make it appear better or of greater value than it is.

"(c) If it bears or contains a coal-tar color other than one from a batch that has been certified in accordance with regulations as provided by Section 406; PROVIDED, That this paragraph shall not apply to citrus fruit bearing or containing a coal-tar color if application for listing of such color has been made under this Act and such application has not been acted on by the Secretary, if such color was commonly used prior to the enactment of this Act for the purpose of coloring citrus fruit.

52 Stat. 1046, § 402, 1 U.S.C.A. § 342.

"(a) Any poisonous or deleterious substance added to any food, except where such substance is required in the production thereof or cannot be avoided by good manufacturing practice shall be deemed to be unsafe for purposes of the application of clause (2) of section 402 (a); but when such substance is so required or cannot be so avoided, the Secretary shall promulgate regulations limiting the quantity therein or thereon to such extent as he finds necessary for the protection of public health, and any quantity exceeding the limits so fixed shall also be deemed to be unsafe for purposes of the application of clause (2) of section 402 (a). While such a regulation is in effect limiting the quantity of any such substance in the case of any food, such food shall not, by reason of bearing or containing any added amount of such substance, be considered to be adulterated within the meaning of clause (1) of section 402(a). In determining the quantity of such added substance to be tolerated in or on different articles of food the Secretary shall take into account the extent to which the use of such substance is required or cannot be avoided in the production of each such article, and the other ways in which the con-

[fol. 289] listing of coal-tar colors.³ Among those eligible for certification were listed F D & C Orange No. 1 F D & C Orange No. 2; and F D & C Red No. 32.⁴ In 1954 the Secretary of Health, Education and Welfare, succeeded to the administration of the Act in the place originally held by the Secretary of Agriculture.⁵ The Secretary reached the conclusion that the three colors are not "harmless" as that word is used in Section 406(b) of the Act. 21 U.S.C.A. §346(b). An order promulgating a further regulation⁶ was issued by which the three colors were deleted from the list approved for certification for use in foods and in drugs to be taken internally. By Section 701 (f) of the Act,⁷ any person who will be adversely affected by an order of the Secretary may file a petition for review with the court of appeals for the circuit wherein such person resides. Petitions for review were filed in three circuits. In the Seventh Circuit the proceeding for review was dismissed. In the Second Circuit, by a decision which we shall hereafter discuss, the Secretary's order was affirmed. *Certified Color Industry Committee v. Secretary of Health, Education and Welfare*, 2 Cir. 1956, 236 F. 2d 866. Two petitions for review have been filed in this Circuit, one by Florida Citrus Exchange and others, orange growers and packers of Florida and Texas, and the other by Frank R. Schell, the holder of patents on the process for the coloring of citrus [fol. 290] fruits with Orange 2 and Red 32. The two proceedings for review in this Court have been consolidated.

Consumer may be affected by the same or other poisonous or deleterious substances.

"(b) The Secretary shall promulgate regulations providing for the listing of coal-tar colors which are harmless and suitable for use in food and for the certification of batches of such colors, with or without harmless diluents." 52 Stat. 1049, § 406, 21 U.S.C.A., § 346.

³ 4 F.R. 1935, 1 C.F.R. 1939 Supp. 1214 et seq.

⁴ 4 F. R. 3936, 1 C.F.R. 1939 Supp. 1214, 1218.

⁵ Reorganization Plan No. 1 of 1953, 67 Stat. 631, 18 F. R. 2053; 67 Stat. 18, 5 U.S.C.A. § 623.

⁶ 20 F. R. 8492.

⁷ 21 U.S.C.A. §371 (f).

Red 32 is the only one of the three colors with which we are concerned in this proceeding.

The three colors were on the original list, prepared in 1939, of coal-tar colors available for certification. Some of the coal-tar colors on the list became suspect as toxic and possibly carcinogenic. This prompted further investigation which culminated in the hearings which formed the bases of the order which we here review. At the hearing evidence was introduced that rats did not survive a diet of 1000 parts per million of Red 32. A dog fed 100 parts per million of Red 32 sickened and ultimately died. This was the lowest percentage tested of Red 32. Evidence was introduced at the hearing which showed that Red 32, when used for coloring oranges penetrated the skin for a depth of about 1/1000 of an inch; that peel of the colored orange had from 17.63 to 34.26 parts per million of color; candied orange peel had 7.4 parts per million of color; orange marmalade analyzed 1.8 parts per million of color; and the squeezed juice of colored oranges had a color content range of from 4/100 of one part per million to 7/100 of one part per million. A spokesman for the entire coal-tar color industry stated that the sale of Red 32 had been discontinued for any purpose except the coloring of oranges. The principal witness for the Secretary was Dr. Vos, Assistant Chief of the Division of Pharmacology of the Food and Drug Administration. He reviewed the tests made upon animals. He testified that on the basis of the experiments and his education and experience he was of the opinion that Red [fol. 291] 32 was not a "harmless coal-tar color". On cross-examination he stated that he used the word "harmless" in the absolute sense that the color was capable of producing harm. This was developed by his saying that bad results might follow the taking of two or three ounces of salt but, salt being essential, it would not be regarded as harmful. He had no evidence as to whether the color would produce harmful effects at ordinary levels of use, although he gave an affirmative answer to the question "Aren't the amount and method of proposed use of a material necessary data for deciding whether the material is harmless for the use intended?"

The order of the Secretary which we here review made findings of fact based upon the evidence of the tests of

which Dr. Vos testified. At the conclusion of nine paragraphs of specific findings as to the effects of the various quantities of the colors given to animals with mention of one episode of illness resulting to man from eating popcorn colored with Orange 1 where the percentage level did not appear, the Secretary stated:

"There was no evidence on which findings could be made concerning how much of the three colors is likely to be ingested by man from his food, drugs, and cosmetics. Some interested persons, taking their own products, attempted to show that the amounts ingested would be small to the point of insignificance. But those contentions leave aside the occurrence of the colors in the products of others, as well as the fact that upon certification of a color the Department has no means of controlling the amounts of colors used in a variety of foods, drugs, and cosmetics. Nor is there authority [fol. 292] to limit a color, once certified, to a single food—for example, FD&C Red No. 32 for use in color-added oranges."

By the order it was determined that Red 32 and the other two suspect coal-tar colors were not harmless and suitable for use in food, drugs and cosmetics and these colors were deleted from the approved list. The legal theory upon which the order was based is found in paragraph 2 of the Secretary's conclusions where it was held:

"Sections 406 (b), 504, and 604 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346 (b), 354, and 364) provide for the listing of coal-tar colors that are harmless and suitable for use in food, drugs, and cosmetics. The act does not provide any method for listing toxic colors for specific food, drug, or cosmetic uses so as to limit their total use to small enough amounts that the toxicity might be disregarded. Under the statute a toxic color cannot be classified as a harmless color."

The primary attack of the petitioners is upon the correctness of the principle as stated in the foregoing quotation.

When the order of the Secretary was entered an effort was made to procure an amendment to the Act to require the Secretary to permit Red 32 to be used in coloring oranges until a more acceptable color should be made available. The amendment as originally offered was opposed by the Department of Health, Education and Welfare. The measure, as finally agreed upon by its proponents and representatives of the Department, amended [fol. 293] Section 402 (c) of the Act by adding thereto the following:

"Provided further, That this paragraph shall not apply to oranges meeting minimum maturity standards established by or under the laws of the States in which the oranges were grown and not intended for processing (other than oranges designated by the trade as 'packing house elimination'), the skins of which have been colored at any time prior to March 1, 1959, with the coal-tar color certified prior to the enactment of this proviso as F.D.&C. Red 32, or certified after such enactment as External O.&C. Red 14 in accordance with section 21, Code of Federal Regulations, part 9: And provided further, That the preceding proviso shall have no further effect if prior to March 1, 1959, another coal-tar color suitable for coloring oranges is listed under section 406". 70 Stat. 512; 21 U.S.C.A. § 342 (c).

While this amendment was pending before the House of Representatives where it had its origin,^a a committee hearing was held. Before the committee was a letter from the Secretary of Health, Education and Welfare where it was stated that the evidence so far available does not establish what the lowest safe dosage of Red 32 would be to test animals, neither does it establish a likelihood of injury to man from the use of the color on the exterior of oranges at the levels of use involved. The studies, said the Secretary, were not designed to determine whether a safe tolerance could be established for a single food, such as oranges, so that the amounts that might be consumed as color on the exterior surface of oranges would pose no

^a H. R. 7732.

[fol. 294] undue risk.⁹ The Commissioner of Food and Drugs appeared and gave a statement at the hearing similar to and in some respects amplifying those contained in the Secretary's letter. He reiterated that the tests made were not designed to learn the effect upon human beings of the minute quantities of the color that might be ingested by its use as an orange coloring. He stated that although the color had been used on oranges since in the early 1930's, no evidence has been found that injury has resulted from the consumption of oranges so colored. This use, said the Commissioner, presented a strong equity for conducting tests. He stated, as did the Secretary, the view of the department that if the color was "harmful" its use must be prohibited and that no tolerances could be fixed.¹⁰ Among the purposes of the amendment, as explained in the report of the Committee of the House of Representatives, was the allowing of time for further exploration of the toxicity of Red 32. In the report it was stated that the practice of coloring the skins of oranges has become an economic necessity for a major segment of the orange industry.¹¹ In the report of the Senate Committee on Labor and Public Welfare, to whom the bill was referred, the same conclusions were reached.¹² On this factual situation and background we review the order of the Secretary.

The petitioners list twelve specifications of error upon which they ground their attack upon the Secretary's order. The basic and underlying contention of the petitioners is [fol. 295] that the Secretary has erred in construing "harmless", as used in Section 406 (b) of the Act, in an absolute rather than in a relative sense. If the position of the Secretary is correct, he has no choice but to refuse to permit a coal-tar color to be used in food in minute, safe and harmless quantities if, when used in much larger quantities it would or might be injurious or dangerous to

⁹ Hearing before a Subcommittee of the Committee on Interstate and Foreign Commerce House of Representatives, 84th Cong., 2d Sess. on H.R. 7732, pp. 2 and 3.

¹⁰ Hearing, *supra*, pp. 17 and 18.

¹¹ H. R. Rep. No. 1982, 84th Cong., 2d Sess.

¹² S. Rep. No. 2391, 84th Cong. 2d Ses.

health. If the position of the Secretary is correct he has no power to permit a particular coal-tar color to be used for a specific and restricted purpose even though, when so used, it would not be injurious or dangerous to health.

The Secretary has urged that the questions presented for our review are the identical questions which were decided by the Second Circuit in *The Certified Color Industry Committee v. The Secretary of Health, Education and Welfare, supra*, and that we should follow that decision unless we are convinced it was clearly wrong. Where an identical issue is presented and no different principle is involved, the decision of another court of appeals is entitled to great weight and affords persuasive argument.¹³ Although the appeal in the *Certified Color Industry* case was from the same order and was upon the same record as the case before us, the identical issue is not presented and a different principle is involved. In the Second Circuit case three coal-tar colors were involved and the uses were all inclusive. The difference was recognized by the Court of Appeals for the Second Circuit. In its opinion it is said:

"Thus the problem is far different from the one presented recently to Congress when the act was amended [fol. 296] to permit the use of Red 32 on orange skins not intended for processing. With only one product contaminated it was not too difficult to argue that such small amounts were involved that a man would have to drink 5000 gallons of orange juice a day before experiencing any adverse effects." 236 F. 2d 871.

The problem we consider is not that which the Second Circuit had and the decision there is, as we hope to show, not in conflict with what we decide here.

In a brief filed with us by *amicus curiae*, he quotes from a letter to him from the Food and Drug Administration where it was said;

"Let me say at the outset that this Administration is in agreement with your conclusion that the use of

¹³ *Sokol Brothers Furniture Co. v. Commissioner of Internal Revenue*, 5 Cir. 1950, 185 F. 2d 222, reh. den. 185 F. 2d 677, cert. den. 340 U. S. 952, 71 S. Ct. 571, 95 L. Ed. 686.

added color is inherently deceptive and is contrary to the interests of both consumers and producers."

This letter is not in the record and would not be the subject of comment by us but for a suggestion that it evidences a hostile and prejudiced attitude of the Food and Drug Administration. We think the record shows the contrary to be the case. It is shown that all oranges to which color is added are so marked and that immature fruit is not colored. The record reflects a departmental attitude of fairness and objectivity, and discloses that the ill-advised statement of the writer of the letter does not express the view of the Secretary or of the department.

[fol. 297]. It has been contended that the officers charged with the administration of the Act had, from the time the Act was passed until the time of the investigation which culminated in the hearings and in the order we here review, construed the Act as permitting, if not requiring, the fixing of tolerance for harmless uses of Red 32. Such administrative construction should be persuasive, so we are told, if not binding as an administrative construction of an ambiguous provision. The Secretary, on the other hand, asserts that the administrative interpretation has not altered, and that the change of position resulted from the different findings of fact required by the recent investigations and experiments. We need not pursue this inquiry. An administrative construction which is clearly erroneous is not binding on the administrative agency nor is it persuasive in judicial proceedings,¹⁴ and this should be particularly true where the purpose of the Act is to protect the health of the public.¹⁵ The doctrine of giving weight to an administrative construction of a statute does not apply to an administrative determination of the administrator's statutory powers.¹⁶ This, in essence, is one of the questions before us.

¹⁴ 82 C.J.S. 771, Statutes § 359 b.

¹⁵ The purposes of the Act are discussed *infra*.

¹⁶ *Stark v. Brannan*, D.C.D.C. 1949, 82 F. Supp. 614, *aff.* 87 U.S.App. D.C. 388, 185 F.2d 871, *aff.* 342 U.S. 451, 72 S. Ct. 433, 96 L. Ed. 497.

The decision we are to make is whether the Secretary of Health, Education and Welfare is required or permitted to determine if there is a minimum quantity of the coal-tar color designated as F D & C Red No. 32 which can be used in adding color to the skins of mature oranges without danger of impairing the health of those who consume [fol. 298] such oranges; and if so required or permitted, and if it be determined that there is such minimum, should the Secretary list and certify such color for such use. In the construction of statutes courts will look to the entire act and to its objects and policy.¹⁷ Results which are incongruous¹⁸ or absurd¹⁹ are to be avoided. Where a particular construction of a statute will occasion great inconvenience or produce inequality and injustice, that view is to be avoided if another and more reasonable interpretation is present in the statute.²⁰ In the construction of a legislative measure, statutes in *pari materia*, amendatory acts, and their legislative history may be examined.²¹ These rules are the primary guides to our solution of the problem before us.

In the leading and often cited Lexington Mill case²² the Supreme Court declares the purpose of the Act, saying:

“The statute upon its face shows, that the primary purpose of Congress was to prevent injury to the

¹⁷ *Mastro Plastics Corporation v. National Labor Relations Board*, 350 U.S. 270, 76 S. Ct. 349, 100 L.Ed. 309, *National Labor Relations Board v. Lion Oil Co., et al*, 352 U.S. 282, 77 S. Ct. —, 1 L. Ed. 2d 331; *United States v. Witkovich*, 353 U. S. 194, 77 S. Ct. —, 1 L. Ed. 2d 765.

¹⁸ *National Labor Relations Board v. Lion Oil Co., et al*, *supra*.

¹⁹ *United States v. American Trucking Associations, Inc.*, 310 U.S. 534, 60 S. Ct. 1059, 84 L. Ed. 1345; *Fulford v. Forman*, 5 Cir. 1957, — R. 2d —.

²⁰ *Knowlton v. Moore*, 178 U. S. 41, 20 S. Ct. 747, 44 L. Ed. 969.

²¹ *United States v. Freeman*, 44 U. S. (3 How.) 556, 11 L. Ed. 724.

²² *United States v. Lexington Mill & Elevator Co.*, 232 U. S. 399, 34 S. Ct. 337, 58 L. Ed. 658.

public health by the sale and transportation in interstate commerce of misbranded and adulterated foods. . . . As against adulteration, the statute was in- [fol. 299] tended to protect the public health from possible injury by adding to articles of food consumption poisonous and deleterious substances which might render such articles injurious to the health of consumers." 332 U. S. 409.

The purpose to protect the public health is an important aim of the statute,²³ and touches phases of the lives and health of people which are largely beyond self-protection.²⁴

We are here reviewing the order of the Secretary only with respect to the coal-tar color F D & C Red No. 32 as used in the coloring of the skins of oranges. If there be other like situations, then of course that which we hold will be applicable to them. We are not confronted with the broad questions which were before the Second Circuit in the Certified Color Industry case, *supra*.

In some of the cases²⁵ the de minimis doctrine has been recognized as applicable or has been applied in adulterated food cases. The contentions of the petitioners suggest that they regard the doctrine applicable here. Neither the Secretary's findings nor the evidence on which they were [fol. 300] based calls for any consideration of the doctrine upon the record before us.

The words "harm", "harmful", and "harmless" are terms of relation. In this sense they resemble "wrong"

²³ United States v. Coca-Cola Co., 241 U. S. 265, 36 S. Ct. 573, 60 L. Ed. 995.

²⁴ United States v. Dotterweich, 320 U. S. 277, 64 S. Ct. 134, 88 L. Ed. 48, reh. den. 320 U. S. 815, 64 S. Ct. 367, 88 L. Ed. 492; 62 Cases of Jam v. United States, 340 U. S. 593, 71 S. Ct. 515, 95 L. Ed. 566.

²⁵ United States v. 449 Cases, 2 Cir. 1954, 212 F. 2d 567, 45 A.L.R. 2d 846; 338 Cartons v. United States, 4 Cir. 1947, 165 F. 2d 728; A. O. Andersen & Co. v. United States, 9 Cir. 1922, 284 F. 542; United States v. 298 Cases, D.C.Ore. 1949, 88 F. Supp. 450; United States v. 184 Barrels, D.C.E.D. Wis. 1943, 53 F. Supp. 652; United States v. 133 Cases, D.C.E.D. Pa. 1938, 22 F. Supp. 515.

and "wrongful".²⁶ Red 32 is harmless, i. e. not harmful, to all persons under the protection of the Act while it remains in the vat or the vial. An injury must occur before harm results. The color Red 32 becomes harmful, i.e. not harmless, when it is consumed, and then only if consumed in such quantity that injury or harm might result. If there can be a use of the color in such small quantities that it can be consumed without risk or injury or harm then, in such quantities, it is harmless. A person is as unharmed after consuming a minute harmless quantity of Red 32 (if such there be) as he would be had he consumed none of it.

In *United States v. Lexington Mill & Elevator Co.*, *supra*, the Supreme Court reviewed the condemnation of a lot of flour to which had been added a poisonous ingredient but in a quantity so small that the health of a consumer could not be thereby injured. The statute then provided that an article of food should be deemed to be adulterated if it "contain any added poisonous or other added deleterious ingredient which may render such article injurious to health". It was contended there, as it is contended here, that it is the character—not the quantity—of the added substance which is to determine the case. This contention was rejected. The Court said:

"If it cannot by any possibility, when the facts are reasonably considered, injure the health of any con-[fol. 301]sumer, such flour, though having a small addition of poisonous or deleterious ingredients, may not be condemned under the act." 232 U.S. 411.

As in the Lexington Mill case, it was held in the Seventh Circuit that "injurious" is a relative rather than an absolute term. *W. B. Wood Mfg. Co. v. United States*, 7 Cir. 1923, 286 F. 84. We think "harmless" is also to be so construed.

The Secretary would concede, apparently, the possibility that a person might consume Red 32 in such small quantities that no hazard to health would result. His guarded statement is that "the evidence so far available does not establish a likelihood of injury to man from the minute

²⁶ Cf *Palsgraf v. Long Island Railroad Co.*, 248 N.Y. 339, 162 N. E. 99, 59 A.L.R. 1253.

amount likely to find its way into the human diet from the consumption of such colored oranges at the level of use involved." ²⁷ The Commissioner of Food and Drugs has admitted that there was no evidence of injury to consumers of colored oranges. ²⁸ The Secretary has made no effort to ascertain whether or not there is, in fact, any likelihood of injury to the health of persons who consume oranges colored with Red 32. Taking the position that no quantitative test is authorized, the Secretary disclaims any power to fix a tolerance for the use of Red 32 in the coloring of oranges or for any other particular use. Under this theory it would make no difference whether or not there was a minimum quantity of Red 32 which would not be injurious. *Malum in uno, malum in omnibus*, is the departmental canon of construction.

[fol. 302] Unless the quantities of Red 32 used in the coloring of oranges are dangerous to public health, the objects and purposes of the Act will not be promoted by a construction which prohibits that use in such quantities. The statute which we construe provides for the fixing of tolerances for added poisonous and deleterious substances required in the production of food ²⁹ and, by a 1954 amendment, ³⁰ for the fixing of tolerances for poisonous pesticides on raw agricultural commodities. We cannot see how the objects and purposes of the statute would be furthered by a construction which permits safe, i. e. harmless, quantities of poisons other than coal-tar colors to be added to food where required in its production, and which permits safe tolerances of poisons for pesticides, but prohibits the use of a coal-tar color in the most minute and harmless quantity because it is harmful and injurious in large quantities. Such a construction would be an unwarranted discrimination, not so much against the coal-tar color and the manufacturers of it, but against that important segment of the orange producers who are economically dependent upon it. The construction of the Secretary results, or may result, in inequality and injustice. There is, we think, a more reasonable interpretation in the Act.

²⁷ Hearing, *supra*, p. 3.

²⁸ Hearing, *supra*, p. 18.

²⁹ 21 U.S.C.A. § 346(a).

68 Stat. 511, 21 U.S.C.A. § 346 a.

The Secretary found that Red 32 is toxic; in other words that it is poisonous. The evidence justified the finding. If the Secretary is correct in his construction of "harmless", Section 402 (a) of the Act is inapplicable to coal-tar colors. If his construction is erroneous, Section 402 (a) would apply. If Section 402 (a) applies, the colored oranges would be "adulterated" only if the added poisonous [fol. 303] substance was unsafe within Section 406 (a). Under this section poisonous substances are permitted to be added to food if it "is required in the production thereof" within such limits as to quantity or extent as the Secretary finds necessary for the protection of public health. The Committees of the Senate and the House of Representatives each found that the practice of coloring oranges has become an economic necessity for a major segment of the orange industry since a high percentage of the oranges grown in Florida and Texas would meet with strong consumer resistance if not colored.³¹ It is as important for a food to be marketable as for it to be palatable and, if the findings of the Committees be correct, then the addition of color is "required in production", as that phrase is used in the Act. Section 402 (a) and Section 402 (c) are not mutually exclusive. A coal-tar color may not be added unless from a certified batch. By Section 406 (b) only those coal-tar colors may be certified which the Secretary has listed as harmless. The Secretary and his colleagues in the Department did not oppose the enactment of the 1956 amendment to Section 40 (c). A reason given was that during the period of the moratorium a "non-toxic color" might be developed. It is the contention of the petitioners that no colors other than Red 32 and the others banned by the Secretary's order are effective. If another color be found which is not a coal-tar color but is as much or more toxic, then we see no reason to doubt that the Secretary would be required to deal with it under Section 406 (a) and to provide tolerances for its use in the event it could be used in any limited quantity without being injurious to the public health. The Secretary, in his order, has stated that "the Department [fol. 304] has no means of controlling the amounts of colors used in a variety of foods, drugs and cosmetics". It is not

³¹ S. Rep. 2891, supra; H. R. Rep. No. 1982, supra.

apparent that this is a problem with respect to other toxic substances which are added to food under tolerances fixed by the Secretary and nothing is shown to indicate that it would be a problem in dealing with a coal-tar color. We see no reason for supposing that Congress intended to permit the use of toxic substances, including toxic colors other than coal-tar products, in safe and harmless quantities and to prohibit the use of toxic coal-tar colors in safe and harmless quantities. We do not ascribe such an intention to Congress. Another reason given by the Secretary for not opposing the 1956 amendment was that the moratorium for Red 32 would permit further exploration of its toxicity. It is the view of the Secretary that if it be found that the coloring of oranges with Red 32 is not injurious to humans and can be continued with safety, further legislation will be required. With this conclusion we do not agree.

We construe the Act as requiring the Secretary, under Section 406 (a), to determine whether the use of the color Red 32 is required in the production for market of oranges grown by a substantial segment of the orange producing industry; and if he finds that such use is so required, then to determine the quantity, if any, that can be tolerated as safe, and by regulation to limit the quantity to such extent as he finds necessary for the protection of public health. With "harmless", as used in Section 406 (b), construed as a relative rather than an absolute term, regulations promulgated by the Secretary under that section as well as under Section 406 (a) could be issued if the prerequisite [fol. 305] findings as to the necessity for using color had been made and the tolerance limits had been fixed.

In the order of the Secretary it is stated that there is no "authority to limit a color, once certified, to a single food—for example, F D & C Red No. 32 for use in color-added oranges". Although there may be no express statutory provision authorizing the limiting of the use of a color to a single food, it is not prohibited. If the adding of a toxic substance to one food may be harmful, but harmless when added to another food in limited quantities fixed by a predetermined tolerance, we are of the opinion that the Secretary is empowered to permit its use in the latter instance. The Secretary at one time seemed of the same opinion. In the Food and Drug Administration Regula-

tions promulgated in 1955, a number of coal-tar colors were listed for certification for use in food, drugs and cosmetics. Among these are colors designated as "lakes". The regulations provide that "No lake listed in paragraph (a) of this section shall be certified for any use in food except external application to shell eggs."³² We shall not indulge in speculation upon the comparative porosity of egg shell and orange peel. We merely observe that the Secretary restricted the use of a group of coal-tar colors to a single food, and we think he was fully empowered to do so.

We are not unmindful of the admonition of the Second Circuit in the Certified Color Industry case, *supra*, that:

"Now that their toxicity has been amply demonstrated it would be unconscionable for any court to require the Secretary to permit their use without the [fol. 306] clearest and most uncompromising evidence that usage at certain levels was absolutely safe." 236 F. 2d 870.

With this statement we are in accord. The findings of fact are to be made by the Secretary. Such findings, under Section 701 (f) (3) of the Act,³³ are conclusive if supported by substantial evidence.³⁴ We again advert to the Secretary's letter to the Chairman of the Committee of the House of Representatives at the time it was considering the 1956 amendment. The Secretary said:

"While the scientific evidence so far available does not establish what the lowest safe dosage would be to test animals, neither does it establish a likelihood of injury to man from the use of this color [Red 32] on the exterior of oranges at the levels of use involved. Before final conclusions can be drawn on this point, however, it is necessary to conduct adequate scientific studies of chronic toxicity on laboratory animals over their life span, which will involve feeding tests at levels related to the quantities of such externally applied color that might enter man's diet. Such tests

³² 20 F.R. 9554, 21 C.F.R. § 9.3 (c).

³³ 52 Stat. 1055, 21 U.S.C.A. § 371 (f) (3).

³⁴ See *Byrd v. United States*, 5 Cir. 1946, 154 F.2d 62.

and studies will require approximately 3 years. We assume that the industry will make such studies."³⁵

Since the Secretary is authorized by Section 702 (a) of the Act ³⁶ to conduct examinations and has a technical staff already familiar with the problem, we think it not amiss, in view of our decision here, that we suggest consideration [fol. 307] be given by the Department to continuing or resuming the tests and studies from which the evidence was obtained which was adduced before the departmental hearing.

In the Certified Color Industry case, *supra*, the court rejected the Secretary's construction of the word "harmless". It holds that the government need not prove that a coal-tar color is in fact injurious to health but it is enough if it shows that it "might render the article of food injurious", adopting the quoted words from the Lexington Mill case. Because, in the quantities tested, the possibility of injury to health was indicated, the court sustained the order. It held that "under the circumstances disclosed in the record" the petitioning manufacturers of coal-tar colors could not require the Secretary to establish tolerances fixing safe levels of use. For this position two reasons were assigned, first that safe levels have not been established, and second, the department could not control use within tolerance limits if such limits were prescribed. In connection with the first of these grounds the court comments that the industry made no investigation as to the effect of the colors at low levels of usage. The record bears out the court's observation, but under the Secretary's construction of the Act the effect of the colors at minimal levels would be immaterial. The inability to control the quantity used is no different, as we see it, in dealing with a coal-tar color than with respect to other toxic or poisonous substances where the Secretary is required to establish tolerances. In any event, as the court in the Certified Color Industry case points out, the situation before it was different from the case of a single color such as Red 32 [fol. 308], applied to a single use such as the coloring of oranges. Such a case is the one before us.

³⁵ Hearing, *supra*, p. 3.

³⁶ 52 Stat. 1056, 21 U.S.C.A. § 372 (a).

After a hearing in 1939 Red 32 was found to be harmless and suitable for use in foods, drugs and cosmetics. The situation as presented on this review was briefly and accurately characterized in a letter from the Commissioner of Food and Drugs to Florida Senators and Congressmen written February 8, 1955. In speaking of Red 32²⁷ the Commissioner said:

"Recent investigations show that these colors when fed in substantial amounts, show evidence of toxicity. There is, however, no evidence that, in the amounts used, and in the manner of use, in the coloring of citrus fruit, the product so colored is not safe for human consumption."

Unless there is evidence that, in the amounts used, and in the manner of use, oranges colored with Red 32 are unsafe for human consumption, the 1939 finding should not be supplanted by a contrary ruling by which such use is prohibited. It may be parenthetically observed that "unsafe" is the yardstick for determining tolerances under Section 406 (a). A determination may be made by the Secretary on his own initiative or upon the petition of any interested person²⁷ as to whether coloring is required and, if so, as to whether Red 32 is a harmless coal-tar color for use in coloring oranges and to fix the tolerances, if any, as may be proper for such use:

[fol. 309] At the outset of this proceeding, upon agreement, a stay order was entered to permit the use of Red 32 in coloring oranges while the proceeding was pending. Except as to duration, the substance of the stay order's provisions is followed in our disposition of the matter.

The order promulgated by Marion B. Folsom, Secretary of Health, Education and Welfare, on November 10, 1955, published in the Federal Register on November 16, 1955, (20 F. R. 8492) will be set aside in so far as said order removes the coal-tar color FD&C Red No. 32 from the list of colors which may be certified for use in coloring the skin of oranges meeting minimum maturity standards prescribed in the State of Florida and Texas;

²⁷ 52 Stat. 1055, 21 U.S.C.A. § 371(e).

provided, that nothing herein or in the judgment of this Court entered pursuant hereto shall restore said coal-tar color to the list of colors which may be certified for unrestricted use in food, drugs and cosmetics but shall operate to authorize the certification of batches of said color conforming to the specifications for the color appearing at 21 C. F. R. 135.3 (1949 ed.) for the purpose of coloring the skin of mature oranges only; provided further, that the Secretary shall be required to certify only sufficient batches of FD&C Red No. 32 as may be necessary to color the skin of mature oranges from time to time; provided further, that the certificates issued for batches of FD&C Red No. 32 may be limited by their certificate for use in coloring mature oranges only; and provided further, that nothing herein or in the judgment of this Court entered pursuant hereto shall be deemed to restrict the Secretary from making further investigations and conducting hearings for a determination of [fol. 310] whether the use of Red is required in the production of oranges and to determine the tolerances, if any, that are safe and harmless, as harmless is herein construed and defined.

Judgment accordingly will be entered setting aside in part, as herein set forth, the aforesaid order of the Secretary.

HUTCHESON, Chief Judge, Dissenting:

I am of the clear opinion that the result reached and the conclusions stated by the majority are unwarranted in law, and also, with respect to the findings of the Secretary of Agriculture, represent a case of judicial fiat which, though it has sometimes found favor in other courts (Cf. *Quaker Oats v. Security*, 129 F(2) 76, reversed 318 U.S. 218), has not until now found favor here. Cf. *Byrd v. U.S.*, 154 F(2) 62.

Because I am of this opinion, I feel constrained not only to note my dissent but to point out as briefly and as effectively as I can the patent errors on which the opinion proceeds. Because, too, it is clear to me that, while certainly presenting matters material for legisla-

tive consideration, it as certainly does not present matters material to the determination of the issue presented here, which is not what the law ought to be but what it is, I pass, with no more than comment, the basic assumption of the opinion, that the effect upon the future of the industry of our construction of the statute is the con-[fol. 311] trolling consideration in this case, to go at once to the controlling issues which are presented for decision here.

The first of these, as stated on page 12 of the majority opinion, is whether the questions presented for our review are the identical questions which were decided by the Second Circuit in the *Certified Color Industry Committee v. Secretary of Health, Education and Welfare* (2 Cir) 1956, 236 F(2) 866.

The second, as the majority opinion states it on page 15 is "whether the Secretary of Health, Education and Welfare is required or permitted to determine if there is a minimum quantity of the coal-tar color, designated as FD&C Red #32, which can be used in adding color to the skins of mature oranges without danger of impairing the health of those who consume such oranges, and, if so required or permitted and if it be determined that there is such a minimum, should the Secretary be required to list and certify such color for such uses".

The third and last, as stated on page 24 of the majority opinion, is whether "If it be found that the coloring of oranges with Red 32 is not injurious to humans and can be continued with safety, further legislation will be required".

I take up these questions in turn to say of the first that I not only find myself in complete agreement with the respondent's position that the decision in the *Certified Color* case is in point, is correct, and should be followed here, but I find completely unconvincing the arguments of the majority in support of its contrary view, that the [fol. 312] case is not in point. Indeed, it seems to me that the fact alone that the orange industry was not a party to the appeal in the *Certified Color* case is, from the standpoint of that case as a precedent, as completely

insubstantial as the classic difference claimed to exist between a white and a black horse case.

In short, the test of what was at issue and decided in, and what was the effect of, the decision in the Certified Color case, as compared to this one, is to be found in a resort to the opinion in that case. Such a resort will show that the precise question here argued, the meaning and effect of the statute, was determined not with particular reference to the nature and character of the business of particular appellants but upon the basis of a construction of the present statute as compared to former statutes, in the light of the decisions construing and applying them. With deference, the majority has completely misread and misapplied the statement in the opinion in the Certified Color case at p. 871, "*Thus the problem is far different from the one presented recently to Congress when the act was amended to permit the use of Red 32 on orange skins not intended for processing*". (emphasis supplied)

In making this statement, the court was not, as the majority in this case seems to think it was, stating that, as applied to oranges, *the construction of the statute under review and the duty of the secretary under it* would be different from the construction of the statute and the duty of the secretary as applied to products generally. In making the statement the court was stating correctly that, viewed from the standpoint of legislative relief by [fol. 313] amendment, the problem presented was different from the one presented to the secretary in proceeding under, and the courts in construing, the statute before it was amended. The court was not at all suggesting that the existing statute gave the secretary any different discretion or authority in respect to oranges than in respect to other products. To have so held would have been in effect to hold that the statute under review here gave the secretary authority in his discretion to consider and determine, product by product, whether he could and should establish tolerances, and this in the face of a statute containing no such language and differently construed both by the Executive or the Legislative branch.

In its treatment of the second question, the majority, acting under the influence of the same idea which dictated

its rejection of the result and the reasoning in the Certified Color case, that the situation and needs of the Texas and Florida orange industry make a special case out of their complaint and requires a construction of the statute based not upon the language used but upon general legislative considerations as to what such an act ought to provide, draws for the support of its view upon the Lexington Mill case, *U.S. v. Lexington Mill & Elev. Co.*, 232 U.S. 399, decided under an entirely different statute, that of 1906, and containing entirely different provisions from those under construction here. It seems clear to me that no sound reason is presented, and no support is found in either the language, the legislative history of the statute under construction, or the authorities cited, for the view of the majority that the Secretary's finding, quoted fully with approval in the Certified Color case at p. 871, was wrong and must be set aside.

[fol. 314] Finally, while the answer of the majority, to the third and final question, whether the needs of the industry can be taken care of without additional legislation, that it can be, follows naturally enough from what has gone before, it seems clear to me that it is nothing more than a complete tour de force, the substitution of judicial for congressional legislation. Though the Executive and Legislative branches of the government have determined that the 1956 amendment to Sec. 402(b) was necessary in order to give the secretary the power to determine tolerances as to coal tar products, the court, differing with both, has held that it can and should by its order in effect say, we will construe the statute, and by order give effect to our construction, so as to make unnecessary, indeed useless, the 1956 amendment or any future congressional legislation, and with the Secretary thus panoplied in the judicial fiat as to his authority under the statute before its amendment, and compelled by the judicial order to give that fiat effect, Congress, the Secretary and the Texas and Florida Industries need trouble themselves no more, but, resting securely upon the judicial legislation and order, they may all go about their business in the future untroubled and undisturbed.

It is one thing for a court to construe a statute. It is quite another for it to rewrite it. I respectfully Dissent

from what I regard here not as a construction but a re-writing of the statute.

[fol. 315] IN UNITED STATES COURT OF APPEALS

No. 15934

FLORIDA CITRUS EXCHANGE, et al.,

vs.

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare.

JUDGMENT—July 12, 1957

This cause came on to be heard on the petition of Florida Citrus Exchange, and others, for review of an order of the Secretary of Health, Education and Welfare issued on November 10, 1955, and was argued by counsel;

On consideration whereof, It is now here ordered, adjudged and decreed by this Court that the order of the Secretary in this cause be, and the same is hereby, set aside in part, in accordance with the opinion of this Court.

"Hutcheson, Chief Judge, dissenting."

[fol. 316] IN UNITED STATES COURT OF APPEALS

No. 15948

FRANK R. SCHELL,

vs.

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare.

JUDGMENT—July 12, 1957

This cause came on to be heard on the petition of Frank R. Schell, for a review of an order of the Secretary of Health, Education and Welfare issued on November 10, 1955, and was argued by counsel;

On consideration whereof, It is now here ordered, adjudged and decreed by this Court that the order of the Secretary in this cause be, and the same is hereby, set aside in part, in accordance with the opinion of this Court.

“Hutcheson, Chief Judge, dissenting.”

[fols. 317-330] Petition for rehearing covering 14 pages filed July 31, 1957. Omitted from this print. It was denied, and nothing more by order. August 28, 1957.

[fol. 331] [File Endorsement Omitted]

IN THE UNITED STATES COURT OF APPEALS FOR THE FIFTH
CIRCUIT

No. 15934

FLORIDA CITRUS EXCHANGE, et al., Appellants,

vs.

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare, Appellee

No. 15948

FRANK R. SCHELL, Appellant,

vs.

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare, Appellee.

On Petitions for Review of an Order of the Secretary
of Health, Education and Welfare.

ORDER DENYING PETITION FOR REHEARING—August 28, 1957
Before HUTCHESON, Chief Judge, and Jones and Brown,
Circuit Judges

Per Curiam

It is ordered that the petition for rehearing in the
above entitled and numbered causes be, and it is, hereby
denied.

HUTCHESON, Chief Judge, Dissenting.

[fol. 332-335] Clerk's Certificate to foregoing transcript omitted in printing.

[fol. 336]

Joint Appendix to Petitioners' Briefs and to Respondent's Brief

IN THE UNITED STATES COURT OF APPEALS, FIFTH CIRCUIT

No. 15934.

FLORIDA CITRUS EXCHANGE, et al.,

versus

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare.

No. 15948.

FRANK R. SCHELL,

versus

M. B. FOLSOM, Secretary of the Department of Health,
Education and Welfare.

On Petition for Review of an Order of the Secretary
of Health, Education and Welfare.

EXPLANATORY NOTE.

By stipulation this is a joint Appendix for the Petitioners in the cases of Florida Citrus Exchange, et al., [fol. 337] vs. M. B. Folsom, Secretary of the Department of Health, Education, and Welfare, No. 15934, and Frank R. Schell vs. M. B. Folsom, Secretary of Health, Education, and Welfare, No. 15948, and on behalf of M. B. Folsom, Secretary of the Department of Health, Education, and Welfare, Respondent in both the foregoing cases.

The figures appearing in brackets to the left of the various pages are references to the pages at which the matter appears in the original record.

[195] Before the Secretary, Department of Health,
Education, and Welfare.

In the Matter of: Amending Sections 135.3 and 135.11 of
the Color Certification Regulations.

Docket No. FDC-60.

Room G-751, Health, Education & Welfare Building,
Washington, D. C., Tuesday, January 19, 1954.

The above-entitled matter came on for hearing, pur-
suant to notice, at 10:00 o'clock a.m.

Before Leonard D. Hardy, Presiding Officer.

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[fol. 338] [200] TRANSCRIPT OF HEARING

Presiding Officer Hardy: Let's call the meeting to order.

On behalf of the Secretary of Health, Education and
Welfare, I would like to welcome you ladies and gentlemen
here today. My name is Leonard Hardy. I have been
designated by the Secretary to hold this hearing in her
stead.

The notice of hearing has been published. It was pub-
lished in the Federal Register for December 19, 1953. I
have five copies here which I will have marked in evidence
as Exhibit No. 1.

(The document referred to was marked Exhibit No. 1 for
identification and received in evidence.)

Presiding Officer Hardy: There are other copies avail-
able and I will pass them around. I don't believe there are
enough for each person, so if you will share your copy with
your neighbor it will facilitate matters.

The purpose of this hearing, as reflected by the notice, is
to receive evidence to determine whether to amend the
regulations for the certification of certain coal-tar colors.
The particular colors designated in the notice and concern-

ing which we will receive evidence are known as FD&C Red No. 32, FD&C Orange No. 1 and FD&C Orange No. 2. [fol. 339] The present regulations are found in Title 21 of the Code of Federal Regulations, Sections 135.1 to 135.15. These [201] regulations include the coal-tar colors which I have just mentioned. The regulations were promulgated originally under the authority of Section 406 (b), 504, 604 and 701 of the Federal Food, Drug and Cosmetic Act.

Those are the same sections which are the basis for the authority for holding the present hearing. Section 406 (b) provides that the Secretary shall promulgate regulations providing for the listing of coal-tar colors which are harmless and suitable for use in food and for the certification of batches of such colors with or without harmless diluents.

Section 504 contains much of the same wording, in fact exactly the same wording, except it provides for the use of these colors in drugs.

Section 604 has exactly the same wording, except that it provides for the listing of colors which are harmless and suitable for use in cosmetics.

So apparently all three fields will be considered. Section 701 is the general authority for promulgating regulations and sets out the manner in which the hearings are to be held.

These hearings are also controlled by the, what is known as the rules of practice for hearing, which are set out in Code of Federal Regulations Section 1.701 through 1.715. Of course, the Administrative Procedure Act is the controlling authority as an Act of Congress, and it is the controlling authority in handling these hearings.

[fol. 340] [202] Now, I have here appearance forms which should be executed in full by all persons intending to participate in the hearing, or who may participate in the hearings. I want to pass these appearance forms around and we will take a few minutes to have these executed and passed back up front so that the record can show the appearance of all persons interested.

(Discussion off the record.)

Presiding Officer Hardy: The Rule of Practice provide for accepting affidavits on or before the date of hearing which are relevant and material to the issues before the hearing, and I would like to know if there are any affidavits that anybody desires to file at this time.

I have received one letter dated January 15, 1954, from McNeil's Laboratories, Inc., which they wish to file in lieu of their appearance at the hearing. The letter is not under oath, and therefore in that respect doesn't constitute an affidavit. The reading of the letter reveals it does not set forth any factual evidence, but merely draws conclusions from data submitted to the McNeil Laboratories by the Food and Drug Administration.

There is nothing in the letter to indicate that the writer, one Robert L. McNeil, Jr., is qualified to make deductions from the data submitted, and therefore I have to rule that this letter is not admissible as part of the record.

[fol. 341] This hearing is held on the initiative of the Secretary [203] of Health, Education and Welfare. Rules of Practice provide that the witnesses or the proponent of proposed amendments shall be heard first. Therefore, the Department's witnesses will go on the stand first.

Mr. Steffy, you are representing the Department?

Mr. Steffy: I am.

Presiding Officer Hardy: Are you ready for your first witness?

Mr. Steffy: I would like to call Dr. Vos to the stand.

Presiding Officer Hardy: Off the record.

(Discussion off the record.)

Presiding Officer Hardy: On the record.

Whereupon, BERT J. Vos, was called as a witness, and having been first duly sworn, was examined and testified as follows:

Direct examination.

By Mr. Steffy:

Q. Will you please state your name?

A. My name is Bert J. Vos.

[fol. 342] Q. What is your address?

A. I live on El Nido Road, just outside of McLean, Virginia.

Q. What is your present position?

[204] A. I am Assistant Chief of the Division of Pharmacology of the Food and Drug Administration, Department of Health, Education and Welfare.

Q. Will you state briefly your educational background and your experience?

A. I have a Bachelor's Degree in Chemistry from the Indiana University, in 1930; a Doctor of Philosophy in Physiological Chemistry from the University of Chicago, in 1934. A Doctor of Medicine Degree from the University of Chicago in 1937.

I interned for one year at the Billings Hospital of the University of Chicago in 1938.

I was an instructor in Pharmacology at the University of Chicago for approximately nine months, and in 1939, in October, I came to the Food and Drug Administration as associate pharmacologist and have been working for the Food and Drug Administration as pharmacologist since then.

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Q. Are you a member of any professional societies, Doctor?

A. Yes, I am a member of the American Society for Pharmacology and Experimental Therapeutics, the Society for [205] Experimental Biology and Medicine, the American Association for the Advancement of Science.

Q. Have you published any scientific publications?

A. I have published approximately a dozen papers on various phases of pharmacology.

[fol. 343] Q. You stated you are Assistant Chief of the Division of Pharmacology of the Food and Drug Administration, is that correct?

A. That is correct.

Q. Would you state briefly your duties in that position?

A. In that position I assist the Chief of the Division of Pharmacology and participate with him in the supervision of the activities of the Division, which includes selecting projects for study, a broad supervision of the set-up of the experiments, and evaluating the results obtained therefrom.

Q. Does the Division of Pharmacology in the regular course of its business keep records of experimental work done in its laboratories?

A. Yes.

Q. Do you have access to these records, Doctor?

A. Yes.

Q. Has experimental work on certified coal-tar colors been carried on in the division of Pharmacology?

A. Yes. We have done considerable work in that field.

.

[206] Q. What was the source of the colors which you used in your experiments on FD&C Orange No. 1?

A. They were obtained from the Division of Cosmetics and from the color certification laboratory which preceded the present Division of Cosmetics.

Q. Is that the Division of Cosmetics and the Color Certification Laboratory of the Food and Drug Administration?

A. Yes, that is correct.

[fol. 344] Q. Who is in charge of that Division at the present time?

A. Dr. Clark. G. Robert Clark.

Q. Has the Division of Pharmacology also carried out experimental work on FD&C Orange No. 2?

A. That is correct.

Q. What was the source of the colors used in this experimental work?

A. It was the same source.

Q. Has the Division of Pharmacology also carried out experimental work on FD&C Red 32?

A. That is correct.

Q. What was the source of the color used in these [207] experiments?

A. All of that color was obtained from the same source as the preceding two, with the exception of two ingredients known as para-isomer and meta-isomer. These were obtained directly from a commercial firm.

Q. Is that a commercial firm ordinarily engaged in preparing FD&C Red 32 for use in foods, drugs and cosmetics?

A. I don't know.

Q. Will you explain the procedure followed by the Division of Pharmacology in conducting toxicity tests on animals?

A. The material to be tested is first selected and then there is a discussion as to the type of animals which should be used in the experiment, the approximate dosage levels on which the experiment should be started, and the experiment is then begun. The work is under the direct supervision of various pharmacologist. The actual administration of the drug to the animals or the mixing of it in test diets is done by technically trained individuals under the supervision of the pharmacologist.

[fol. 345] The animals are examined daily—perhaps I should say, inspected daily. Any unusual appearance of the animals is immediately called to the attention of the pharmacologist in charge, and as the experiment progresses the results are discussed with the various members of the Division, including myself.

[208] Q. Was this customary procedure followed in conducting experiments with FD&C Orange 1?

A. Yes.

Q. Is that also true of the experiments conducted with FD&C Orange 2, and FD&C Red 32?

A. That is correct.

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[215] By Mr. Steffy:

Q. In addition to the tests which you have described which were performed on animals, Doctor, have you had any personal experience with FD&C Orange No. 1?

A. Yes. Several years ago a sample of candy was collected by an inspector of the Food & Drug Administration as a result of a complaint that the candy had caused diarrhea in a child. This sample of candy was tested by us in the Division of Pharmacology. When we administered it to rats we observed no [216] adverse effects. When it was tested on human volunteers, of which I was one, there was produced a marked abdominal griping and diarrhea. In my own case the results were obtained with 6 or 8 pieces of the candy. In some of the other volunteers who ate the candy, 4 pieces caused the diarrhea in one

person, and diarrhea was produced by 1 piece of candy in one person.

[fol. 346] As a result of testing the various ingredients of the candy, we gradually narrowed the cause of the diarrhea down to the coal-tar colors which were used to color the candy, and finally to the individual color, FD&C Orange No. 1. When this color was tested on several individuals, doses of 100 or 80 milligrams, as a single dose, produced the marked griping and diarrhea which the candy itself had produced.

[217] Q. In connection with your duties at the Division of Pharmacology, have you also had occasion to conduct tests on FD&C Orange No. 2?

A. I have.

Q. Do you have with you the reports of the tests conducted on FD&C Orange No. 2?

A. I do.

Q. Would you hand me a copy of that report. Doctor, the report you handed me is entitled, "Chronic Toxicity of FD&C Orange No. 2 in Rats". At least that is the title of the first page. The report consists of 18 pages. In this document a report on all of the toxicity tests on animals conducted on FD&C Orange No. 2, since that color was admitted to listing?

A. Yes, it is.

Mr. Steffy: I ask this report be marked as Exhibit 3 for identification.

Presiding Officer Hardy: It may be so marked.

(The document above-referred to was marked Exhibit No. 3 for identification.)

[fol. 347] [218] Presiding Officer Hardy: Off the record.

(Discussion off the record)

Presiding Officer Hardy: On the record.

By Mr. Steffy:

Q. Doctor, will you briefly outline the nature of the experiments which are reported in Exhibit 3 for identification?

A. The first experiment was begun in 1939 and consisted of a two-year feeding test in rats, in which 24 rats were

placed on a diet containing 500 parts per million of FD&C Orange No. 2 mixed in a diet called Diet "A", which is described in the exhibit. A second group of 24 rats received the same diet without the added color in a parallel 2-year experiment. Groups of 18 rats were fed 500 parts per million and 100 parts per million of FD&C Orange No. 2 mixed in a low-protein diet, and a third group of 18 rats received the low-protein diet alone.

The original growth and mortality data on these two experiments is no longer available. The mortality data has been taken from the files of the pathologist and shows no effect on mortality as a result of feeding FD&C Orange No. 2 at these two levels.

However, in the examination of the animals by the pathologist, it was noted that there were changes in the hearts of the animals which had received 500 parts per million of FD&C Orange No. 2 in their diet, both in the animals on Diet "A" and in the animals in the low-protein diet. There was a [219] suggestion of certain other changes at the 100PPM—parts per million level, but occurred in only two animals.

[fol. 348] The next experiment on FD&C Orange No. 2 was begun in 1940. In this experiment 10 rats were fed a diet containing FD&C Orange No. 2. The concentration was 0.1 percent for the first 8 weeks of the experiment. After this the concentration was increased to 0.2 percent for the remainder of the experiment.

Table 1, on page 5, shows a marked depression of the growth of the animals as compared to the controls. There was no mortality during the first 8 weeks, but after the concentration was increased to 2/10 of a percent, deaths began to occur. 7 of the rats were found dead between the 9th and 22nd week of the experiment, and 3 were sacrificed in poor condition between the 13th and 17th weeks.

The median survival time is shown in Table 1. The control rats, half of them survived for 101 weeks whereas the median survival time for the animals on FD&C Orange No. 2 was only 15½ weeks. Pathological examination of the animals showed principally abnormalities in the livers. The changes are described as either focal coagulation necrosis, or a more diffuse subacute type of degeneration, or both.

Q. Will you state for the record, Doctor, where those changes are recorded in Exhibit 3 for identification?

A. The description is on the bottom of page 3 and the top of page 4.

[220] The next experiment is described on page 6 of the exhibit. In this experiment FD&C Orange No. 2 was incorporated in the diet of rats. Five rats were given a diet containing 0.1 percent of the color, and 10 rats were given a diet containing 0.25 percent of the color. Additional 5 animals served as controls and received a diet without added color. The results of the experiment are shown in Table 1, on page 6. There was a severe retardation of [fol. 349] growth at the .25 percent level, a marked retardation at 0.2 percent.

At the higher level there was an increased mortality of the animals, and the experiment was discontinued at the end of the 42nd day because of the mortality on the higher level. No pathological examination was made of these animals because they had been on the diet for such a short time.

The next experiment is described on page 7 of the exhibit. It was begun in 1953 and consisted of the subcutaneous injection of 18 rats with 0.1 milliliters of a 5 percent suspension of FD&C Orange No. 2 in glycerine. The injections were made subcutaneously once a week. Control animals were injected with glycerine alone. The object of this experiment was to determine if the color, when injected in this manner to rats, led to the production of tumors at the site of the injection. One of the rats which received the color died following 7 injections. A second died after 8 injections. And the injections were discontinued. A third rat was found dead 11 [221] days after the final injection of FD&C Orange No. 2. There were no deaths among the control animals. The experiment was discontinued after 8 injections because of the toxic effects.

The next experiment is described on page 8. It was begun in 1940 and involved subcutaneous injection of FD&C Orange No. 2 into two groups of 18 mice. The amount of color injected each time was 12.1 milligrams. The injections were made with a modified trocar into the right axillary region, subcutaneously.

The injections were made at irregular intervals, 8, 19, 24, 30, and in one case, 55 weeks after the initial injection.

There were no tumors seen at autopsy by gross examination of the animals.

[fol. 350] The next experiment, which is described on page 9 of the exhibit, was begun in 1938 and involved the administration of FD&C Orange No. 2 to dogs. The first dog received 100 milligrams per kilogram per day in gelatin capsules for a period of about 11 months. Following this the dose was reduced to 20 milligrams per kilogram per day and was continued for 60 months. The second dog was started on 100 milligrams per kilogram per day given as an oil solution by stomach tube for about a month. The dose was then reduced to 20 milligrams per kilogram per day for about a month, and finally to 5 milligrams per kilogram per day administered in capsules. This dose was continued for 62 months.

[222] In the case of the first dog the dose was reduced from 100 milligrams because the dog was in poor condition as a result of this dose. When the dose was reduced to 20 milligrams per kilogram per day the color was tolerated and the dog gained weight. It was sacrificed in good condition after 60 months on this dose. The dose in the second dog was reduced, first from 100 milligrams per kilogram per day to 20 milligrams per kilogram per day, and finally to 5 milligrams per kilogram per day because the dog was not eating well, and was gaining weight slowly on the higher doses. The 5 milligrams per kilogram per day was tolerated and the dog was sacrificed apparently in good condition after 62 months on this dose.

In this period of time the dog had 6 litters of puppies, which were of average size and health.

Examination of the dogs after sacrifice, revealed only the moderate atrophy of testis and prostate of the male dog, and since this is an isolated observation, no significance is attached to it.

[fol. 351]- The next experiment started as described on page 11. This experiment was begun in 1953 and involved the administration of FD&C Orange No. 2 to dogs. Four dogs were started on a diet containing 0.2 percent of the color. They showed diarrhea for the first few days on this diet. They ate poorly, lost weight steadily. On the 28th day of the experiment two of the dogs were sacrificed in ex-

tremis. They had lost respectively 43 and [223] 32 percent of their initial weight. The remaining two dogs had lost 31 and 21 percent of their initial weight, respectively. They were placed on a normal diet for 9 days, and during this rest period, they regained some weight and improved their physical condition. Then with two additional dogs they were placed on a diet containing 0.04 percent FD&C Orange No. 2. On this diet the four dogs did well for about a month. Following this they began to eat poorly and lose weight. On the 75th day of this concentration the first of the four dogs was found dead. The second was found dead on the 95th day. The third was killed in extremis on the 98th day. The 4th was found just at death, on the 124th day. All four dogs had lost approximately 50 percent of their body weight prior to death.

Pathological examination of the animals showed emaciation. One dog had a moderate amount of fluid in the peritoneal and pleural cavities. On microscopic examination the basic pattern was atrophy and/or cellular depletion of the various organs; the most frequently being affected was the liver, spleen, bone marrow, genital organs, skeletal muscle, and lymph nodes.

In the final experiment on this color, which is described on page 18 of the exhibit, was conducted in 1952. In this experiment 5 of the 11 dogs which had been found sensitive [fol. 352] to the cathartic action of FD&C Orange No. 1 were tested with FD&C Orange No. 2. The drug was administered at a [224] dose of 200 milligrams per dog in capsular form. All 5 of the dogs developed diarrhea within 8 hours after the administration of the capsules.

Q. Does Exhibit 3 for identification contain a complete summary of these tests which you have described, including the pathological results?

A. Yes, it does.

Q. Are the original data sheets available for inspection for any interested parties?

A. With the exception of the first experiment described on page 1, for which the original data sheets have been destroyed—the original data sheets of the remainder experiments in the exhibit are available.

OFFER IN EVIDENCE

Mr. Steffy: I ask Exhibit 3 for identification be received in evidence.

Presiding Officer Hardy: Is there any objection? Let it be so received.

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[225] Mr. Steffy: Has Exhibit 3 been received in evidence?

Presiding Officer Hardy: Is there any objection to the admissibility of Exhibit 3 in evidence? It may be so received.

By Mr. Steffy:

Q. On the basis of the tests reported in Exhibit 3, and on the basis of your education, training, and experience, [fol. 353] do you have an opinion as to whether FD&C Orange No. 2 is a harmless coal-tar color?

A. I do.

Q. What is that opinion?

A. It is my opinion that it is not a harmless coal-tar color.

Q. In connection with your position in the Division of Pharmacology, have you had occasion to conduct experiments with the coal-tar color known as FD&C Red No. 32?

A. We have.

Q. Do you have with you reports of those experiments?

A. I do.

Q. Is the report to which you refer a 29-page report, the first page of which bears the title, "Chronic Toxicity of FD&C Red No. 32 in Rats"?

A. It does.

Mr. Steffy: I ask that this report be marked as Exhibit No. 4 for identification.

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[226] By Mr. Steffy:

Q. Doctor, will you outline briefly the nature of the experiments which are reported on in Exhibit 4 for identification?

A. The first experiment was begun in 1940 and is reported on page 1. It shows that a 0.1 percent concentration

of FD&C Red 32 in the diet of rats markedly depressed the growth and reduced the median survival time.

[fol. 354] The second experiment is reported on page 2. It was begun in 1941. It shows that 0.1 percent of FD&C Red No. 32 retarded the growth of rats and reduced the median survival time.

The pathological examination of the rats in the two preceding experiments is described on page 3. It shows an effect on the liver of the rats treated with the color. The principal changes are bile duct proliferation, hyperplasia of the hepatic cells, irregularly mixed with areas of atrophy, and moderate or marked central lobular hepatic cell necrosis.

The next experiment was begun in 1951 described on page 4. In this experiment FD&C Red No. 32 was added to the [227] diet of rats at various concentrations. At a 2 percent level all rats were dead within 7 days. At a 1 percent level all died within 12 days. When weanling rats were given 0.5 percent they died within 21 days. Slightly older rats given 0.5 percent, 3 of the 5 were dead in 26 days, the remaining two were sacrificed when their weight decreased. At 0.25 percent two rats died in 7 and 6 weeks, the remaining 3 were sacrificed at the end of 10 weeks.

[228] This experiment was begun in 1952 and involves the feeding of FD&C Red No. 32 in the diet of the rats. The results show that there is a marked effect on mortality at a level of .25 per cent, a less pronounced effect on mortality at 0.1 per cent, a marked retardation of the growth in both groups.

Moderate to severe anemia, depending on the dose, and an increase in the white cell count.

[fol. 355] Pathological examination of the rats in this experiment is described on pages 8 to 17 of the exhibit. The outstanding features were moderate to marked liver damage at the 0.25 per cent level of the diet, slight to moderate liver damage and heart lesions at the 0.1 per cent level of the diet.

[229] The next experiment is described, beginning on page 18 of the exhibit. It was begun in 1953, and involved the testing of FD&C Red No. 32 for carcinogenicity injection into rats. In the first experiment the weekly dose was gradually increased to approximately ten milligrams per rat and resulted in such toxicity that the experiment was discontinued.

The table 1 shows the blood count of the animals which received the color, and it shows marked anemia as the experiment progresses. The counts shown for the ninth week were taken 12 days after the last injection and show a beginning improvement in the count.

In the second experiment, which was set up for the same purpose, it was set up in conjunction with a similar test of FD&C Orange No. 2, and when that latter color showed evidence of toxicity the entire experiment was discontinued since the experiment had been set up with litter-mate animals. When the one part was stopped the entire experiment was stopped.

In neither of those two tests was the experiment conducted [230] long enough to reach any conclusion as to the possibility of carcinogenicity by repeated subcutaneous injection of rats.

[fol. 356] The next experiment is described on page 20, and consists of the subcutaneous injection of FD&C Red No. 32 into mice at irregular intervals. There was in this experiment no evidence of carcinogenicity found.

The next experiment is described beginning on page 21. It was begun in 1938 and involved the administration of FD&C Red No. 32 to dogs. Five dogs received a dose of five milligrams per kilogram per day for a period of five to six years, and were sacrificed at the end of this period in apparently good condition.

One of these dogs had received a dose of one hundred milligrams per kilogram per day for approximately a month, which was later reduced to 20 milligrams per kilogram per day for approximately a month. An additional dog received one hundred milligrams per kilogram per day for about ten months and was later put on 20 milligrams per kilogram per day which was continued for approximately five years.

In addition, one of the constituents of FD&C Red No. 32, the para-isomer was administered to two dogs at a

dose of five milligrams per kilogram per day for six years and the meta-isomer was administered to three dogs at a dose of five milligrams per kilogram per day also for six years. .

The two dogs which received one hundred milligrams per [231] kilogram per day of FD&C Red No. 32 showed moderate weight loss, while this dose was being given.

Pathological examination of the animals following sacrifice showed no changes which would be attributed to treatment.

The next experiment is described starting on page 23. It was begun in 1953 and involved the administration of FD&C Red No. 32 by incorporating it in the diet of dogs. Four dogs were started on a level of 0.2 per cent of [fol. 357] the color. Two of these were sacrificed at the end of 26 days after they had lost 28 and 29 percent of their weight. The other two dogs were placed on a control diet for ten days, and then after they had regained weight and improved their condition they were placed with two additional dogs on a diet containing 0.01 per cent of FD&C Red No. 32.

One of those four dogs lost approximately 60 per cent of its body weight and was found dead after 173 days on the diet. The remaining three dogs have lost some weight, but appear in fair condition after approximately ten months on this diet. The four dogs were fed 0.04 per cent of FD&C Red No. 32 in their diet. They lost weight up to about 50 per cent and were sacrificed in extremis at 124, 137, 148 and 148 days on the experiment. There was sporadic diarrhea observed during the experiment.

The pathological examination of these dogs is described on pages 24 to 28 of the exhibit. The findings were slight or [232] moderate pallor of the organs and tissues in general, gelatinous bone marrow, and atrophy of the liver as judged by gross examination.

The microscopic examination, the principal feature was atrophy and/or cellular depression of the various organs, such as the liver, spleen, lymph nodes, bone marrow, genital organs, and skeletal muscle.

The final experiment in FD&C Red No. 32 is described on page 29. It was conducted in 1952. Ten dogs which had previously been found sensitive to the cathartic action

of FD&C Orange No. 1 were tested on FD&C Red No. 32. When they were given two hundred milligrams of FD&C Red No. 32 per dog, eight of the ten developed diarrhea. Five dogs were later tested with a dose of one hundred [fol. 358] milligrams per dog, and four developed diarrhea and one gave questionable results.

[233] Q. On the basis of the experiments which you have described, and which are reported in Exhibit 4, and on the basis of your education, training, and experience, do you have an opinion as to whether FD&C Red No. 32 is a harmless coal-tar color?

A. I do.

Q. What is that opinion?

A. My opinion is that it is not a harmless coal-tar color.

[235] Q. Dr. Vos, I noticed in Exhibit 2, 3, and 4 you specify the levels of feeding in different terms, sometimes in percentage, sometimes in milligrams per kilo, and other times in parts per million.

I wondered if we could convert some of those things into something we are familiar with. In percentage, that would be simple enough, that is just arithmetic, isn't it?

A. Yes.

Q. In those parts of your exhibits where you talked about milligrams per kilo, I was not able to find the amount of the diet, and is there any basis to at least approximate those levels in values of parts per million?

A. It could be done accurately only by referring to the actual amount of diet which the animals ate and then computing it in those terms. Of course, the material was given in a single dose, it was not diluted through [fol. 359] the diet, so the two experiments are not strictly comparable, as they are both toxicity experiments, but in one case the material was given in a single dose and in the other experiment it was diluted in the diet.

Q. I see.

[236] A. As a rough approximation, in the case of rats, if you will—in the case of young rats—if you will multiply the milligrams per kilogram per day by ap-

proximately ten, you will get a figure which corresponds to parts per million in the diet.

Q. Could you make a like assumption in the case of dogs for estimate purposes?

A. The discussion which I just had before applies as to the difficulty of relating the two experiments, but for a rough approximation, if you multiply the milligrams per kilogram per day, in the case of dogs, by a figure of approximately 40, you will—

Q. That will give you parts per million roughly.

A. That will give you roughly parts per million per diet. That is based on the average consumption of food by dogs.

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Q. Well, while we are on that page, I notice those percentages there, while it is only arithmetic, but for convenience [237] may we go down the line.

2.0 per cent would mean 20,000 parts per million, is that correct?

A. Yes.

Q. That is the third line?

A. Yes.

Q. And 0.5 per cent would be 10,000 parts?

A. Five thousand.

[fol. 360] Q. No, one per cent would be 10,000 parts, and 0.5 per cent would be 5,000, and so on, down the line. Can you tell us the rationale on the basis on which you select these levels, and the other levels in the experiment that you had?

A. No. These were simply levels that were selected after a consideration of some extent of work which had been done previously, and an attempt was made here to cover quite a wide range of dosages which would give a clue to a proper dose or set of doses to select in a subsequent experiment.

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A. In general, in a toxicological study we attempt to administer the compound under investigation at a series of levels, [238] some of which will produce no effect, some a slight effect, and others a marked effect. Obviously, in

some of these experiments where the color was given at only one dosage level in the experiment it would be impossible to achieve all of those ends.

Q. Well, then, these levels were not specifically related to the levels of these colors as actually used under normal conditions of use?

A. No, that was not a part of this.

Q. Have you any evidence at such levels where the capacity for producing harmful effects was tested at levels of ordinary normal conditions of use?

A. I have very little information on the matter of what the customary levels of use are.

[fol. 361] Q. Well, as I understood it, you didn't need that for your purposes?

A. That is right.

Q. Because your tests were not related to that at all. About that candy incident: Do you know what the level of the [239] dye was in that candy?

A. I understand that it was seven-hundredths of a per cent.

Q. Seven-hundredths of a per cent. That would be approximately a million?

A. Seven hundred parts of a million.

By Mr. Markel:

Q. Dr. Vos, then, you have no evidence as to the capability of producing harmful effects of any of these colors at the level of ordinary use under normal conditions of use, I should say?

[240] A. Without having a more thorough information on the actual level of ordinary use I would hesitate to answer that question.

Q. Well, you have no evidence at levels other than the levels appearing in the exhibits?

A. That appear in the exhibit, that is correct.

Q. Aside from the experiments that you have referred to here, do you know of any other evidence of injury to humans except this child that ate this candy as you have described?

A. It is my impression there was a second report of injury with this same candy. I have been unable to locate that report so that as I say that is my impression that there was a second instance reported while we were investigation the first sample.

[fol. 362] Q. But except for this specific candy instance, you have no information?

A. That is correct.

[241] By Mr. Holloway:

Q. Dr. Vos, have you conducted any tests or experiments other than by feeding or by direct injection into an animal to determine the effect of the subject colors?

A. No, I have not. Perhaps I might amplify that. We are in the process of setting up experiments in which we will study [242] the effect of these colors applied topically. The experiment is just in the process of beginning, and we have no results at all to date.

Q. You have no tests or form no conclusion of the use of subject colors for use on the skin or in any cosmetics?

A. That is correct.

Q. Including lips?

A. That is correct.

Q. When you, in response to a question, which was based on your experiments and the tests and your own experience, the question being whether or not in your opinion you considered each of the three subject colors harmless, and you stated that in your opinion they were not harmless.

Were you using the term "harmless" then in the absolute sense that each of the colors were capable of producing harm?

A. That is correct.

Q. In that sense, then, is not common salt capable of producing harm?

[fol. 363] A. Well, I believe in the case of common salt you have to take into consideration the fact that it is essential to live, so that since you can't get along without some salt, I don't think you could ordinarily consider salt harmful.

Q. Nevertheless, if you took salt in a quantity of two or three ounces, you may get some bad results from salt?

A. There would be some adverse effects from two or three [243] ounces of salt, yes.

Q. Then all your experiments and tests tended to show some resulting harm depending on the quantity fed?

A. That is correct, or injected.

Q. Or injected?

A. Yes.

Q. That is, when it was fed in certain percentages or certain dosages or in certain percentages of the diet?

A. That is correct.

Q. Or in relationship of the weight of the animal fed?

A. Yes.

Q. Are the bases of your experiments, and the test experiments, been, that you have no basis of an opinion as to harmfulness when any of the subject colors are used for other than feeding or injection?

A. That is correct.

• • • • •
Cross-examination.

By Mr. Kleinfeld:

Q. Dr. Vos, I think you testified in answer to Mr. Markel's questioning that you were not familiar with the [fol. 364] particular levels which might be used in a particular food, is that correct?

[244] A. Substantially so, yes.

Q. Now, did your answers to Mr. Markel change your opinion as to whether FD&C Red No. 32 was a harmless coal-tar color?

A. No, it did not.

Q. Did the questioning and your answers change your opinion as to whether Orange No. 2 was a harmless coal-tar color?

A. No.

Q. Mr. Holloway asked you questions about whether almost any substance might not cause some adverse reactions, for example, salt, and I think you said that if sufficient quantities, even salt might produce some adverse physiological reactions, is that correct?

A. That is correct.

Q. Let's take some other substances. For example, will you consider carbolic acid a harmless substance?

A. No, I would not.

Q. Could I possibly use such an infinitesimal portion of carbolic acid in a food so that no one would be injured by eating that food?

A. I am uncertain as to what amount of carbolic acid can be added to food without causing injury to any persons. There is animal information on the toxicity of carbolic acid, however.

Q. Is it conceivable you might use such an infinitesimal amount of carbolic acid or strychnine in a food so that a [245] person eating that particular food would not be injured in any respect?

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[fol. 365] Q. Dr. Vos, if we assume that a substance like strychnine or carbolic acid might be used in a food in such a minute amount as not to cause injury to a person eating that particular food, would that change your opinion as to whether carbolic acid or strychnine was a harmless substance?

A. No, it would not.

[246] Q. Would your opinion still be the same that carbolic acid, for example, was a harmful substance, even though a certain slight percentage might be used in a particular food so as not to cause harm in a person consuming it?

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Dr. Smith: My name is William E. Smith. I am Associate Professor of Industrial Medicine at New York University, Secretary of the Cancer Prevention Committee in New York, Chairman of the Committee on Cancer Prevention for the International Union against Cancer.

I am here in connection with my service on these two committees. I believe it may be pertinent to make some mention of their composition to establish the substantial nature of their interest in the hearings.

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[247] By Dr. Smith:

Q. The first is: If he could give us any indication of the possible extent of the problem that he has been—the practical extent of the problem he has been studying, in that we would be interested in learning the amount of [fol. 366] the dyes that are the subject of this hearing that have been certified by the Government for use in foods within the past few years.

I should also like to submit, if you wish to accept, a copy of the proceedings of the Cancer Prevention Committee which was published as a special issue of the A.M.A. Archives of Industrial Hygiene and Occupational Medicine in 1952.

[248] Q. My next question refers to the tests that the witness has described for cancer producing action of the dyes. I note that on page 71 of the proceedings of the Cancer Prevention Committee, a copy of which I am prepared to submit, reference is made to tumors of the liver produced by a dye described—

Mr. Holloway: I must object to that.

[249] Q. Whether the witness for the Government feels that the studies that he has described on the tests for possible cancer-producing action of these dyes constitute, in his mind, full [250] and satisfactory evidence for the absence of such activity on the part of these dyes, and I ask the question in view of findings in the literature—

The Witness: I would say that the experiments which we have conducted are not complete with respect to the question of whether the three coal-tar colors under consideration [fol. 367] are capable of producing cancer under any circumstances.

[252] By Mr. Holloway:

Q. Dr. Vos, aren't the amount and method of proposed [253] use of a material necessary data for deciding whether the material is harmless for the use intended?

A. May I hear that question again, please?

(Question read.)

The Witness: I would say yes.

[255] Presiding Officer Hardy: Will the witness explain how he used "harmless" on the witness stand? In what manner did you use the term "harmless", in a pharmacological sense, or as a conclusion of law under the Food and Drug Act?

The Witness: I used it in pharmacological sense.

Presiding Officer Hardy: That is the way you used it all through your testimony, is that correct?

The Witness: That is right.

[fol. 368] [256] Q. The purpose of my question is to see what the witness' understanding of the question was, so I think the only question addressed to the witness is, how did you understand Mr. Holloway's question? What was the meaning of your answer?

Presiding Officer Hardy: I think we are just likely to get more involved. I suggest, Dr. Vos, you answer Mr. Holloway's question, and anybody that wants to clear it up on further cross-examination or further direct will be given the opportunity. You have heard Mr. Holloway's question. I think you made an answer. Is that the answer you desire to make to his questions, is that still the answer.

[257] The Witness: Yes. The amount of the dye, of the color, has to be considered in determining whether or not it is harmless.

[258] Re-Cross Examination.

By Mr. Holloway:

Q. You use a substance in several ways. You apply it to the skin, you take it internally, you gargle with it, you use various methods of application?

Presiding Officer Hardy: With that explanation in mind, Dr. Vos, can you answer his question?

The Witness: I think it is appropriate the method of use should be taken into consideration. The dyes in question [fol. 369] are at present being certified for use in foods, drugs, and cosmetics, and the data which we presented in these exhibits have shown that they are not harmless for use in all of those products. As I have pointed out, we have no data as to whether they are or are not harmless for external application.

[259] Q. Doctor, I think you can see inherent—you have indicated, I think you can see an inherent good in your answer, since you state that you have made no experiments or have no experience for the use of the subject colors in cosmetics, or for application to the skin. And then at the same time you imply that your experiments have indicated to you that the application of the colors to the skin are not harmless.

Q. In view of that, will you please explain your answer?

A. I don't recognize the ambiguity which you refer to. As I see it, these drugs, these colors are, as I say, at present certified for use in foods, drugs and cosmetics, and the proposal is to withdraw them from certification for those three purposes, and the evidence shows that the colors are not harmless under certain conditions. The question of whether they are harmless under certain other specified conditions, namely for external application, is as yet unanswered.

[260] A. My opinion as to harmlessness does not apply to external application. In other words, I have no opinion as to the harmlessness of these colors by external application.

Q. Would you include in external, the lips?

[fol. 370] A. Well, I believe it is commonly recognized that colors which are applied to the lips are to a greater or lesser extent swallowed, which is the route of administration by which these colors were found to be not harmless.

Q. Doctor, I am trying to get straight in my own mind, perhaps it may help others, whether we are talking about a harmless substance or a harmless amount of a substance. It seems to me they may be quite different things. For example, you have testified that in your opinion, based on your training and experience, and on the data which you have submitted here, FD&C Red No. 32 was not a harmless coal-tar color, is that correct?

A. That is correct.

Q. Now would your opinion be changed if an amount of Red [261] No. 32 was used in or on a particular food product in an amount less than those amounts which you utilized in your experimental work? If you use a lesser amount than the amounts used in your experimental work, and for example, you did not and could not observe any deleterious or harmful effects in a person or a test animal, in testing the food with the smaller amounts of Red 32, would you then say, in your opinion, Red 32 was a harmless coal-tar color?

A. No, I would still regard it as a harmful color on the basis of the tests which we have conducted.

Q. Isn't there any difference from the viewpoint of pharmacologists and toxicologists between a harmless substance and a harmless amount of a substance?

A. That is correct.

[fol. 371] [262] By Mr. Markel:

Q. Can you tell us in what sense you have used the term harmless, by defining the term?

A. I have said that these colors are not harmless in the

sense that they did cause harm to the experimental animals in the experiments which are listed here.

Q. And in answer to one of my questions also, you have no evidence it would cause harmful effects in quantities used under ordinary conditions of use?

A. With the exception of the—

[263] Q. Candy incident—

A. Candy incident.

Re-direct examination.

By Mr. Steffy:

Q. Doctor, you have asked concerning the term milligram per kilogram, and how you converted it to grams per millions. In the experiments reported in Exhibits 2 to 4, is it true where you use the term milligram per kilogram, that the substance upon which you were reporting was given in capsule form at those times?

A. Well, it was given by several routes of administration. In many instances it was given in capsule form; in some cases it was given by stomach tube, as an oil solution. In other instances it was injected. Milligrams per kilogram refers to milligrams per kilogram of body weight of the animal.

Q. Then where you use milligrams per kilogram, it was not given in the diet but was given separately, is that correct?

[fol. 372] A. That is correct.

Q. Where you used parts per million, that is where the substance was included in the diet as a whole?

A. Where we said parts per million, or percent of the [264] diet, that is where the substance was included in the diet.

Q. In your opinion, Doctor, do the experiments reported in Exhibits 2 to 4 show a possibility of harmful effect upon humans of the coal-tar colors used in those experiments?

A. There is certainly a possibility. As to how great a possibility there is, it is a matter of speculation, I would say.

Q. Do you have any evidence to show that FD&C Orange 1, or Orange 2, or Red 32, are harmless when applied topically?

A. No, I do not.

Q. On cross examination you were also asked concerning the toxicity of carbolic acid. I believe you stated that you know generally the level of chronic toxicity of carbolic acid on certain animals, is that correct?

A. That is correct.

Q. Could you give an approximation of the comparison of the chronic toxicity of Red 32 with carbolic acid?

A. Carbolic acid is tolerated in the—

[265] Mr. Kleinfeld: The point is, it seems to me we are trying to establish whether a particular substance, let's say Red 32, is or is not a harmless substance. Now unless you can go to the dictionary and use that definition, when people [fol. 373] brought in substances like salt, it seems to me perhaps the best way of determining from a pharmacologist viewpoint whether a substance is harmless or not, how it compares in toxicity with comparable substances. I can't think of a better way, myself.

[266] The Witness: From the standpoint of chronic toxicity, when administered in the diet of rats, carbolic acid is tolerated without adverse effects at concentration of 1 or 2 per cent. On the other hand, Red 32, as shown in these experiments, had an adverse effect on growth and survival at concentrations of 1/10 of 1 percent, or greater.

[272] Q. Well now, your answers have already brought out that the LD-50, the 22 substances is quite different. It is much higher for Red 32, by that meaning much less, it takes much more of Red 32 to produce comparable effect than it does carbolic acid, isn't that true?

A. By single administration that is right—by oral administration.

Q. By single administration?

A. That is correct.

Q. And on repeated feeding the animal tolerates much more carbolic acid?

A. That is correct.

Q. How can you make a comparison?

[fol. 374] A. Well, there are several types of toxicity. There is acute toxicity and there is chronic toxicity. One substance, "A", can be more toxic than "B" acutely, but chronically, it can be reversed. That is the situation you have here.

Q. But nevertheless you can take column 2 and 2, and get 4 out of it. In other words, nevertheless you feel you can make those comparisons, notwithstanding the differences?

A. Well, I believe that both types of toxicity have to be taken into consideration. If the thing is acutely toxic, it is certainly not harmless. If it is chronically toxic, it is also [273] certainly not harmless.

[274] The Witness: Edwin L. Gustus. I am here today representing the Bjorksten Research Foundation of Madison, Wisconsin. Should I give my background?

Presiding Officer Hardy: Give a brief summary of your qualifications, Doctor.

The Witness: I was graduated in Chemistry from Stanford University in 1921, following which I took a Master of Science Degree in Northwestern University, and taught in the Medical School there for two years in the biochemistry department.

Subsequently, I took a Doctor of Philosophy Degree in organic chemistry at Northwestern University, and then served five years on the Rockefeller staff of Medical [fol. 375] Research in the Department of Pharmacology. Subsequently, I went to Europe as an International Education Fellow, and studied with Professor Ruzicka, the Nobel Prize Winner, at the Swiss Technical Institute. I then returned to the United States to the Pennsylvania State University. Subsequently again a guest [275] worker at the Rockefeller Institute for Medical Research, and then subsequently to that I have been bio-chemist in the drug industry with two firms.

I am not a physician, and I am not strictly speaking a pharmacologist. The statement I have to read this afternoon is a broad one and not specific particularly to

the dyes that we have discussed, but to dyes in general belonging to these groups.

[276] over this statement, that appears to be a statement of general conclusions based on rather—apparently rather extensive investigation of literatures and what not, and affects the whole chemical industry, not only all the difficulties here but it cuts clear across the board of this whole question which is at the moment highly controversial. As much as I regret to object to statements made by people who come in and want to make statements, but because of its character I must object unless all the underlying data on which these conclusions were based is produced here as a basis for this statement, and if need be I am perfectly willing to consent to a recess of sufficient proportion so that the doctor can get his material together, but I feel that it is not fair to the whole industry, not only the industry which I represent, but other industries, to put such general conclusions in a record of this character, without backing them up.

[fol. 376] Presiding Officer Hardy: Mr. Markel, I believe the statement is relative. The weight to be given it is entirely a different question. The lack of foundation or experimental data would go certainly to the weight to be given the statement. But I believe—Doctor, let me ask you one or two questions.

What is the Bjorksten Research Foundation?

The Witness: It is a foundation supported by private funds, and is dedicated to the investigation of certain bio-chemical phenomena, associated with age. We have up to date [277] been studying the deposition of cholesterol in the arteries, largely with the idea of trying to obtain some insight in the changes which occur in the arteries with aging, but in going through our literature studies we have become aware of the fact that substances occur in the diet of man which may not be in the diet of experimental animals, and that it might be worth our while to consider—

[278] The Witness: Workers at the Bjorksten Research Foundation have recently been engaged in reviewing the

literature on biochemical processes which may be involved in the various manifestations of human aging. Our attention has been attracted to the effects which chemical substances, commonly added to food materials or likely to contaminate food products, may have on such processes. We are very much aware of the paucity of reliable experimental evidence on the effects of very long continued ingestion of certain of these additives and the [fol. 377] difficulty of translating results from animal experiments to the question of human health.

Among those chemical substances in this group which are purposefully added to foods, we feel that the certified coal tar dyes deserve a great deal of further study and that their harmlessness over the very long term may well be questioned.

We feel that there is a great difference between a material which the public can avoid by the exercise of free choice and one which necessarily finds its way into the daily diet of a [279] great majority of the population. It is this inability of the public to avoid by choice the ingestion of certified food dyes that makes the question of their harmlessness over many years of daily ingestion one of the most important tasks which come within the responsibilities of the Food and Drug Administration. It is imperative that the public, and not the food dyes, be given the benefit of any doubt.

In recognizing that this right of choice is effectively denied to the consumer, dyes which have found their way to the certified list should not be allowed to remain there if any reasonable doubt, however slight, exists about their long term harmlessness.

We are exceedingly happy to see that the Division of Pharmacology of the Food and Drug Administration is giving much attention to this question and we feel that their request that certain dyes be eliminated from the certified list is decidedly in the public interest. We hope that these investigations of certified food dyes will be continued and extended to include those dyes frequently used for coloring foods of general daily use. Such dyes should be given the most careful and prolonged study, especially in regard to their possible cumulative effects, and they [fol. 378] should be promptly removed from the certified

list if there is found to be the slightest reason to doubt their harmlessness over a lifetime of daily ingestion.

[280] Cross-examination.

By Mr. Markel:

Q. If I suggest to you the dye manufacturers operate exactly as you suggest, that if there is any question about harmfulness, they stop making and stop merchandising. I am suggesting that to you. Do you have any information to the contrary?

A. No. I only know the harmlessness of certain dyes was as far as I am concerned amply demonstrated by the testimony here today. I hope, therefore, that the dye manufacturers will indeed follow the thing which you say is their principle.

[287] The Witness: My name is Robert C. Evans. I am General Manager of the Florida Citrus Commission, with headquarters at Lakeland, Florida.

[290] The Witness: The Florida Citrus Commission has interested itself in this hearing because we understand that one of the colors here under consideration, Red 32, is the principal color used in coloring oranges. Therefore, the Commission, at a meeting held January 6, directed that I and its Director of Research, Dr. L. G. MacDowell, appear [fol. 379] at this hearing and present certain factual data, that may be helpful to the Food and Drug Administration.

I wish to state that our appearance here is not to be construed that the Commission opposes any action which the Secretary may deem advisable on the basis of the record of this hearing. Neither are we appearing to take a position for [291] or against the artificial coloring of oranges because it is our understanding from the notice of the hearing in the Federal Register that the merits of coloring oranges or not coloring oranges are not involved in this hearing.

[293] Direct examination.

Presiding Officer Hardy: Will you state your full name?

The Witness: Louis Gardner MacDowell.

Presiding Officer Hardy: You are also—

The Witness: I am Research Director of the Florida Citrus Commission, Lakeland, Florida.

[295] The Witness: This report was prepared by Dr. S. C. [296] Ting, a Research fellow of the Florida Citrus Commission, and directed to myself. The work was done at my direction.

[fol. 380] To save time in the testimony I would prefer to skip over the thing fairly rapidly and start out by saying that under sampling that two boxes of color-added pineapple oranges, size 216, were obtained from a commercial packing house in Hope County, Florida, that is, and all analyses in this report are based on these fruits. . .

Reading from page 12, Table 9, a summary table on the concentration of dye on color-added oranges and in products made from color-added oranges, we find that whole fruit analyzed by extraction and chromatographic separation ranged from 3.39 to 4.69 parts per million of dye per fruit. Whole fruit by a chloroform washing method, which is outlined in the procedure, ranged from 4.96 to 6.78 parts per million. Peel of fresh fruit by the extraction and chromatographic separation, ranged from 17.63 to 24.39 parts per million. Peel of fresh fruit analyzed by the chloroform washing method analyzed from 25.79 to 34.26 parts per million. Juice extracted from whole fruit which had been color-added, and extracted on two types of commercial extractors, ranged from .04 to .07 parts per million of dye.

Candied orange peel analyzed 7.4 parts per million. [297] And orange marmalade analyzed 1.8 parts per million.

[322] Will you state your name?

The Witness: C. Boyd Shaffer.

[fol. 381] Direct Examination.

By Mr. Markel:

Q. What is your occupation, Mr. Shaffer?

A. I am Chief Industrial Toxicologist of the American Cyanamid Company.

Q. Is that company a manufacturer of one or more of the colors here under consideration?

A. They are.

Q. Has the industry, the coal-tar color industry, organized a committee for the purpose of considering the problems raised by the consideration of the coal-tar colors listed in the notice of this hearing?

A. Yes, they have organized such a committee, and I am chairman of that committee.

Q. How many manufacturers does the committee speak for?

A. The committee speaks for nine basic manufacturers of coal-tar colors. That constitutes the entire industry.

[323] Q. Now, you have indicated you would like to make a statement for the record as Chairman of this Committee. Will you proceed to make that statement?

A. I might say at the outset that the coal-tar color industry has conducted no further pharmacological investigations of these colors since they were admitted to the list for certification in 1938. When certain experimental data was called to our attention last year by officials of the Food and Drug Administration there did not remain sufficient time for use to undertake any further investigations of our own. That circumstance will explain the fact that we have no—the industry has no pharmacological data of its own to submit at this hearing.

[fol. 382] It was the judgment of the Committee that if any doubt existed as to the potentiality or harm of these colors, that the primary manufacturers would refrain from submitting further batches of these colors for certification. Therefore, the primary manufacturers have ceased submitting any further batches of the 3 colors in question for certification with the exception that we are submitting, and shall continue to submit so long as it remains certifiable, FD&C Red No. 32 for the sole purpose of the coloring of oranges. There is no sale at present of Red 32 for any other purpose.

Q. May I interrupt at that point? Have the interested members of the industry given written assurances to that effect [324] to the Food and Drug Administration?

A. The American Cyanamid Co., which is my employer, has written the Food and Drug Administration that we have discontinued the sale of Red No. 32 for any other purpose but the coloring of oranges, and insofar as the other manufacturers are concerned, I have by word of mouth, assurance that they are not selling the color for any other purpose. I do not know that such intention was expressed in writing to the Food and Drug Administration.

The reason that we continue to sell FD&C Red No. 32 for the coloring of oranges is that having the knowledge of the amount and distribution of the color in the fruit, and in products prepared from the fruit, we believe that human consumption is negligible.

[fol 383] [325] Q. You said, Dr., some months ago, when your Committee was informed, the Food and Drug Administration advised you that these three colors were in question as to their toxicity?

A. Yes, sir.

By Mr. Kleinfeld:

Q. Dr. Shaffer, has your company conducted any pharmacological work on the 3 colors which are at issue here?

A. We have conducted pharmacological work on FD&C Red No. 32.

Q. When did you perform that work?

[326] A. It was done in 1938.

Q. Have you done any work since then?

A. We did a 90-day feeding study of the dye, in 1952.

Q. Did you bring with you the data?

A. No, sir, I did not.

Q. Is there any reason why you didn't?

A. There is no reason why I did not.

Q. You performed no additional work since that particular type of work which you just mentioned, is that right?

A. That is correct. There was no additional work.

Q. Do you know whether—

A. I might say, Mr. Kleinfeld, we regard that small amount of work, the 90-day feeding study, as rather insufficient to establish the point one way or the other. That is why I neglected that, in saying to all intents and purposes, we have done no further pharmacological work.

Q. Why did you perform it?

A. Why did we?

[fol. 384] Q. Yes.

A. We intended to carry out, it was the first step in the program of more extensive studies, but with the data developed by the Food and Drug Administration we saw no reason to complete further studies, or to undertake further studies.

Q. Are you willing to accept the result of the studies made by the Food and Drug Administration?

[327] A. Yes, we do.

Q. Do you know whether any of the other companies, comprised in your Committee, whether they have done any pharmacological work on these 3 colors?

A. They have not since 1939. I am quite confident about that.

Q. Has the American Cyanamid Company performed any independent work in trying to discover how much of these colors is found in various foods, including oranges and products made from orange peel, on which these colors may have been employed?

A. No, sir, we have not.

EXHIBIT 3

Chronic Toxicity of FD&C Orange No. 2 In Rats

(1939)

In a two-year experiment 24 rats, including both sexes, were fed 500 ppm FD&C Orange No. 2 mixed in a diet called "Diet A." This diet consisted of natural foodstuffs such as whole cer-al grains, leguminous seeds and milk solids, fortified by the addition of mineral constituents and accessory food factors required by the rat for adequate growth. [fol. 385] A second group of 24 rats received the same diet

without added color and served as controls. In a parallel two-year experiment two groups of 18 rats, of both sexes, each were fed 500 ppm and 100 ppm respectively, of FD&C Orange No. 2 mixed in a low-protein diet. This diet consisted of 72% starch, 6% casein, 6% corn oil, 5% yeast, 5% whole liver powder, 4% salt mixture and 2% cod liver oil. A third group of 18 rats received this low-protein diet without added color and served as controls for this experiment.

The growth data and the original mortality data on these two experiments have been discarded, but adequate mortality data was taken from the pathologist's files. There was no effect on mortality, survival of the two-year experiment being 9 of 24 for the Diet A controls and the same number for the treated rats; 6 of 18 for the low-protein diet controls, 8 of 18 for those fed 500 ppm dye, and 6 of 18 for those fed 100 ppm.

Department of Health, Education and Welfare

Exhibit No. 3.

Hearing FDC-60.

Offered by: Government.

Date 1/19/54.

Reporter TWB.

[fol. 386] Gross and relatively detailed microscopic pathological examination was done on the above animals as follows:

	Number Started	Not Rec'd	Gross and Micr. Exam.	Gross Exam. Only
Diet A controls.....	24	2	21	1
Diet A, 500 ppm.....	24	2	21	1
Low protein Control.....	18	0	15	3
Low Protein 500 ppm.....	18	3	12	3
Low protein 100 ppm.....	18	1	13	4

The low-protein diet caused such lesions as fatty change in the liver, and hairballs in the stomach, in both control and treated animals. Because most of the animals were 1½ to 2 years of age, the animals on both diets showed a number of tumors and other incidental lesions such as slight bile duct proliferation in the liver, nephritis, testicular

atrophy, etc. Only in the heart could a definite difference between treated and control animals be made out. Right ventricular hypertrophy was seen either grossly or microscopically (usually both) in 6 of the rats on 500 ppm in Diet A, in 7 of those on the same level in the low-protein diet, in 2 at 100 ppm, and in none of either control group. The 2 instances at 100 ppm were slight in degree, whereas those at 500 ppm averaged moderate. By themselves the 2 instances at 100 ppm could not be called significant. The livers of the 500 ppm group on diet A had suggestively more of the common slight old-age changes, especially bile duct proliferation, than did the controls; in the low-protein group any effect of the color was obscured by that of the diet. [fol. 387] Also, this same 500 ppm Diet A group showed 3 instances of slight hepatic cell hypertrophy or hyperplasia, which changes were not noted in any of the other groups.

Chronic Oral Toxicity of FD&C Orange No. 2 in Rats (1940)

Method: Five male and 5 female rats were fed a ground commercial animal laboratory diet to which FD&C Orange No. 2 was added. For the first 8 weeks of the experiment, the concentration in the diet was 0.1%. It was then increased to 0.2% for the remainder of the experiment. The rats were 21 or 22 days old at the start and weighed from 25 to 50 grams. They were housed in individual cages, given free access to food and water, and were weighed at weekly intervals. This experiment was conducted simultaneously with the 1940 test on FD&C Red No. 32 and the same group of control rats served for both experiments. The results on these control animals are repeated here to facilitate comparison.

Results: As shown in Table 1 the addition of 0.1% FD&C Orange No. 2 to the diet of rats markedly depressed their growth. When the level was increased to 0.2%, deaths began to occur. Seven of the rats were found dead between the 9th and 22nd week of the experiment; 3 were sacrificed because of poor condition between the 13th and 17th week. Seven of the 10 control rats survived to the end of the experiment. (101 or 102 weeks.)

Gross and microscopic pathological examination was made of 6 treated and 5 control animals, and only gross examina-

tion of 3 additional treated and 4 additional control animals. (The controls also were controls for FD&C Red No. [fol. 388] 32.) The treated rats had been on the experiment for 10 weeks to 5 months, and the controls for 46 weeks to 2 years. The liver was markedly affected in the treated rats, whereas the control livers were almost unaffected. Grossly, the control livers showed no abnormalities, whereas 5 of the 9 treated ones did. There were 3 instances of yellow or red mottling, 1 of pallor, and 1 of slight enlargement. Microscopically, the total changes in the 5 controls examined were 1 instance of slight diffuse atrophy and 1 of slight hepatitis. In the 6 treated animals which were sectioned, all livers showed either focal coagulation necrosis, a more diffuse subacute type of degeneration, or both. The total process was marked in degree in 4, moderate in 1, and slight in 1.

Table 1

Weight and Mortality of Rats Fed a Diet Containing FD&C Orange No. 2

Dosage	Sex	No. of Rats	Weight, gm		Medium Survival Time Weeks
			Initial	8 Weeks	
0%*	M	4	39	365)	101
	F	5**	33	216)	
0.1% for 8 weeks	M	5	35	140)	15½
0.2% thereafter	F	5	42	122)	

* These are the same control animals reported in the the 1940 FD&C Red No. 32 experiment.

** Data sheet on one female rat is missing.

[fol. 389] Subacute Oral Toxicity of FD&C Orange No. 2 in Rats

(1952)

Method: Male weanling rats of the Cabern-Mendel strain weighing between 45 and 55 grams were fed 0.1% and 0.25% of FD&C Orange No. 2 in a basic diet of commercial ground laboratory chow for a total of 42 days. Ten rats were fed the higher level while five each were fed 0.1% and control basic diet without the color.

Rats were caged individually, allowed free access to food and water and weight gains and feed intake were recorded once during each week of the experiment.

Results: The data given in Table 1 show that FD&C Orange No. 2 retarded growth severely when fed at 0.25% and markedly when at 0.1% in the diet. Weight gains are given for 35th day because controls lost weight during the last week when their food cups were not filled. The higher level produced death of 20% of the animals by the third week and 40% by the fifth week. It became apparent that animals could not tolerate 0.25% of the color and the experiment was terminated on the 42nd day.

Table 1

Weight and Mortality of Rats Fed FD&C Oranges No. 2

	Sex	No. of Rats	Average Initial Weight gm.	No. of Rats	Average on 35th Day Weight gms.	Wgt Gain gms.	Mortality 42 Days
Control.....	M	5	43	5	202	159	0%
0.25%.....	M	10	50	8	74	24	40%
0.1%.....	M	5	47	5	130	83	0%

[fol. 390] Test of FD&C Orange No. 2 For Carcinogenicity
by Repeated Subcutaneous Injection in Rats

(1953)

Method: Nine male and 9 female (7-week old) rats were injected subcutaneously once a week with 0.1 ml. of a 5% w/w suspension of FD&C Orange No. 2 in glycerin. Nine males and 9 females which were litter mates of the above rats were similarly injected with glycerin alone and served as controls for both this experiment and the second experiment of this type on FD&C Red No. 32.

Results: As shown in Table 1 the weekly injection of approximately 5 mg. of FD&C Orange No. 2 depressed the growth of the rats. One of the treated rats died following 7 injections; a second died after 8 injections and the injections were discontinued. A third rat was found dead 11 days after the final injection of FD&C Orange No. 2. There were no deaths among the control animals. Since the experiment was discontinued after 8 injections because of toxic effects no conclusion was reached as to the possible carcinogenic action of the color.

[fol. 391]

Table 1

Weights of Rats Injected with a Glycerin Suspension of FD&C Orange No. 2 or with Glycerin

Injection	No. of Rats	Sex	Average Weight—Gm.		
			Initial	5 weeks	8 weeks
FD&C Orange No. 2	9	M	196	295	300**
	9	F	147	187	195**
Glycerin*	9	M	193	335	384
	9	F	145	203	222

* These rats are the same ones which served as controls in the similar experiment on FD&C Red No. 32.

** Average of eight survivors.

Carcinogenicity Tests in Mice With FD&C Orange No. 2 (1940)

The color was made into a glycerin paste and inserted by means of a modified trocar into the right axillary region subcutaneously of 18 C-57 black mice (8 males and 10 females #181-198) and of 18 swiss white mice (18 males #199-216). Each mouse received 12.1 milligrams of the color each injection. The first injection was made 10-3-40 and 10-8-40 for the two groups respectively and repeated 8, 19, 24, 30, and 55 weeks thereafter except for the C-57 group which did not receive the 55-week injection. The remaining 5 mice in this group had been autopsied 39 weeks after the first injection. No tumors were seen at autopsy by gross examination.

[fol. 392] A similar set of control mice was used. See FD&C Red No. 32.

Chronic Oral Toxicity of FD&C Orange No. 2 in Dogs (1938-1944)

Method: In this experiment two dogs received FD&C Orange No. 2 in gelatin capsules daily except Sunday. The first dog, a male, received the dry color in the capsules at a dose of 20 mg. per kg. per day for 60 months. It had previously received 100 mg. per kg. per day for about 11 months. The second dog, a female, received a dose of 5 mg. per kg. per day of the color dissolved in oil and placed in capsules for 62 months. It had previously received doses

of 100 mg. per kg. as an oil solution administered by stomach tube daily for about a month, followed, after a rest period, by doses of 20 mg. per kg. per day administered as an oil solution in capsules for about a month.

Results: The 100 mg. per kg. per day dose of the male dog was discontinued because the dog was in poor condition. When the dose was reduced to 20 mg. per kg. per day after an approximate one-month rest period the color was tolerated and the dog gained weight. It was sacrificed in good condition after 60 months on this dose. The dose of the female dog was reduced from 100 mg. per kg. per day to 20 mg. per kg. per day and finally to 5 mg. per kg. per day because the dog did not eat well and was gaining weight slowly on the higher doses. The 5 mg. per kg. per day dose was tolerated and the dog was sacrificed in good condition [fol. 393] after 62 months on this dose. In this period it had six litters of puppies which were of average size and health.

Following sacrifice these two dogs were examined grossly and in relative detail microscopically. They were normal for their age except that the testis and prostate of the 20 mg. dog were moderately atrophic. Since no other dogs at this dosage level were available for examination no significance can be attached to the observation.

Chronic Oral Toxicity of FD&C Orange No. 2 in Dogs (1953)

Method: This color was fed at levels of 0.2% and 0.04% in the diet. A basic diet of ground laboratory chow was used. Each dog was housed in an individual metabolism cage, fed and watered daily and given free access to his food. Each dog was weighed approximately weekly. A total of six young adult dogs evenly divided as to sex was used.

Results: The four dogs which were started on the diet containing 0.2% FD&C Orange No. 2 showed diarrhea which lasted for only a few (3-4) days. All ate poorly and lost weight steadily. On the 28th day of the experiment two of the dogs were sacrificed in extremis. They had lost respectively 43% and 32% of their initial weight. The remaining two dogs, which were in poor physical condition and had lost respectively 31% and 21% of their initial

weight, were placed on a normal diet for nine days. During this time they regained some weight and improved their physical condition. Along with two additional dogs they [fol. 394] were placed on a diet containing 0.04% FD&C Orange No. 2. On this level all four dogs did fairly well for about a month; following this they began to eat poorly and lose weight. On the 75th day the first of the four dogs was found dead. The second was found dead on the 95th day. The third was killed in extremis on the 98th day. The fourth was found just at death on the 124th day. All four dogs had lost approximately 50% of their body weight prior to death.

Pathological Changes in Dogs from Feeding of FD&C Orange No. 2

Path No.	Dog No.	Sex	Appr. Age, No.	% Dye in Diet	Days on Expt.	F.D.** or K.	Weight in Kg. Beg.	End
15710	B-6	F	34	0.20	27	K.	5.8	3.8
15711	105-263	M	9.5	0.20	27	K.	10.0	6.8
16032	M-302-2	F	15	0.04*	75*	F.D.	9.2	4.2
16097	M-293	M	35	0.04	95	F.D.	19.8	8.1
16118	105-264	F	11	0.04	98	K.	9.8	4.8
16352	M-305	M	26	0.04*	124*	F.D.	16.5	8.8

* After 27 days on 0.20%; weight during that time dropped from 11.7 to 8.0 kg. for 16032, and from 19.4 to 15.3 kg. for 16352.

** (Illegible) sacrificed because of poor condition.

Gross Pathology

15710—Marked emaciation; very little body fat. Viscera essentially negative. No worms.

15711—Slight to moderate emaciation. One to 2 dozen [fol. 395] roundworms up to 6 cm. long in upper portion of small intestine. Viscera essentially negative otherwise.

16032—Marked emaciation; moderate dehydration. No body fat. Liver firm and contains little blood; slightly atrophic and pale. Spleen pale red and bloodless. Uterus slightly distended; thin-walled. No worms. Bone marrow gelatinous. Thyroid pale. Tissues as a whole appear slightly anemic.

16097—Marked emaciation. Liver slightly atrophic, with a fine nutmeg appearance. Spleen pale and bloodless. No worms. Bone marrow somewhat gelatinous. Advanced post mortem autolysis.

16118—Marked emaciation. Tissues in general slightly anemic. Liver firm, medium brown color, slightly atrophic. Spleen purplish red. About 1 dozen roundworms up to 7 cm. long in upper portion of small intestine. Bone marrow congested.

16352—Moderate emaciation. Peritoneal cavity contains about 100 cc. of clear, straw colored fluid; about 50 cc. of same in pleural cavities. Tissues in general appear anemic. Liver slightly atrophic, medium chocolate brown in color, slightly soft, and contains little blood. Kidneys slightly soft; dark tan color. Spleen bloodless; has a slight grayish tan tinge. No worms.

Microscopic Pathology

Because of advanced post mortem autolysis, microscopic examination of 16097 was limited to liver, kidney and bone marrow, including fat stains and smear respectively. From [fol. 396] each of the remaining 5 dogs, hematoxylin-sosin stained paraffin sections of formalin-fixed tissues were made from lung, heart, liver, gall bladder, spleen, pancreas, lymph nodes, kidney, adrenal, stomach (2), small intestine (3), colon, thyroid, parathyroid (except 15711), urinary bladder, voluntary muscle, testis (or ovary), prostate (or uterus), submaxillary salivary gland, and rib bone and marrow; also, from each of these 5 dogs frozen sections of kidney and liver were stained for fat with Oil Red O, a smear of bone marrow was stained with Giensa type stain, and paraffin sections were made of liver and kidney fixed in Zenker's fluid. Some adrenals were also stained for fat and/or had portions fixed in Zenker's fluid. All of those sections were normal or essentially so except as follows.

Atrophic Changes in Various Organs: This was the basic pathological pattern. For convenience, the most consistent and easily graded of these changes are shown in tabular form, and the degree of bodily emaciation is repeated. In the table, 1-slight, 2-moderate, and 3-marked or severe. The changes in the bone marrow and to a lesser extent in the spleen and lymph nodes, are a depletion of certain cells rather than actual shrinkage in size of the organ or of its component cells, but the term atrophy is often used and generally understood, and for convenience it is used here. In the skeletal muscles,

there were changes (nuclear multiplication, necrobiosis, necrobiosis), in addition to the atrophy, so that the total muscle lesion is a dystrophy rather than simple atrophy. Of the organs not listed, atrophic changes in the uterus were the most noticeable.

[fol. 397] The figures in the table have no mathematical exactness for comparative purposes because of subjective factors, differences in the atrophic process among various organs, and the difference between depletion and atrophy mentioned above. Because of the great liability of the bone marrow, a few words of explanation about it may help. Our dog rib marrows, on the average, normally are made up of (by inspection, not measurement) about $\frac{1}{3}$ hematopoietic (plus a small percentage of stromal) cells, about $\frac{1}{2}$ fat cells, and the remainder by, chiefly, capillary blood vessels. In determining these values the artefacts of shrinkage spaces, and the relative unobtrusiveness of fat cells in routine paraffin sections, have been considered. The moderate bone marrow depletion shown in the table means a reduction in hematopoietic cells of around 50% of the normal.

Pathology No.	Bodily Emaciation	Liver	Spl.	Lym.N.	Mar.	Test.	Pro.	Muscle
15170	3	1-2	1-2	1	1-2	Fem.	Fem.	1
15711	1-2	0	0	0	\pm	2-3	3	\pm
16032	3	3	2	1	3	Fem.	Fem.	2
16097	3	2-3	N.S.	N.S.	2-3	N.S.	N.S.	N.S.
16118	3	\pm	2	1	\pm	Fem.	Fem.	1
16352	2	2	1-2	2	\pm Hy.	3	3	2

Abbreviations in last 6 columns mean respectively Spleen, Lymph Nodes, Marrow, Testis, Prostate, Female, Not Sectioned, and Hyperplastic.

Changes Other than Atrophy and/or Cellular Depletion: Stainable fat in the liver was shown to a very slight degree in 3 of the 6, the greater part of this being in [fol. 398] the Enpffer cells. In the kidney, stainable fat was greater in amount, but was within normal limits, the females showing more than the males as is commonly the case. Hemosiderin in from very small to moderate amounts was present in the liver and bone marrow of the last 4 dogs in the tables. In the spleen, hemosiderin was on the whole present in slightly greater than usual amount, but there was no relation of this

excess to dosage or duration. In the bone marrow, the myeloid/erythroid ratio was determined only by inspection, not counting. In 16118 and 16352 it was reduced, appearing to be less than 1. In 15710 and 15711 it appeared slightly increased. Mature granulocytes were greatly reduced in 16097, 16118, and 16352. Atypical cells of apparent reticular derivation were noted in 15710, 16032, and 16352. The changes mentioned for this phase of the marrow examination indicate a definite effect of treatment on the marrow, but no consistent relation to time or dosage can be made. Certain changes in the skeletal muscles were previously mentioned; both these and the atrophy were greater in the thigh than in the neck muscles. Of the 5 stomachs sectioned, that of 16118 showed moderate enlargement and rarefaction of the fundis parietal cells.

The positive findings mentioned in the above paragraph can be attributed to treatment, as, of course, are the atrophies previously mentioned. Certain other changes, scattered among the various organs and none of major proportions, cannot be attributed to treatment; these are listed on the work sheets filed with the copy of this report in the pathology laboratory.

[fol. 399]

Summary and Conclusions

Gross and microscopic pathological examination has been made of 6 dogs fed FD&C Orange No. 2 (Orange SS) at either 0.20% or 0.04% or both dosages, for periods of 27 to 151 days. Three of the dogs were found dead and the remaining 3 were sacrificed because of poor condition.

On gross examination, the only external change of significance was consistent emaciation, usually pronounced and varying from slight-moderate to severe. Internally, the common changes were slight atrophy of the liver, and slight pallor (anemia) of the tissues in general. One dog had moderate amounts of fluid in the peritoneal and pleural cavities. Two dogs had intestinal worms.

Detailed microscopic examination was done on 5 of the 6 dogs, and some on the remaining one. The microscopic picture was consistent, the basic pattern being that of atrophy and/or cellular depletion in various organs, the

most frequently affected being liver, spleen, bone marrow, genital organs, skeletal muscle, and lymph nodes. In general, these atrophies paralleled the degree of emaciation. In addition, the changes attributable to treatment included dystrophic changes in skeletal muscle in addition to the atrophy there, changes in type and percentage distribution of bone marrow cells in addition to the depletion, slight hemoriderosis of the liver and bone marrow, a very small amount of fatty change in the liver, and, probably, changes in the mucosal cells in one stomach.

[fol. 400] On the whole, the effects from FD&C Orange No. 2 were very similar to those from FD&C Red No. 32, reported on January 4, 1954. Chemically the two dyes are also very similar, FD&C Red No. 32 having an additional methyl group on one of the rings.

Cathartic Action of FD&C Change No. 2 in Dogs

(1952)

Five of the eleven dogs which had been found to be sensitive to the cathartic action of FD&C Orange No. 1 was tested on FD&C Orange No. 2. In this test they were fasted over night. The next morning they were given a capsule containing 200 mg. of FD&C Orange No. 2. They were fed about 2 hours later. All five dogs developed diarrhea within eight hours from the administration of the capsules.

EXHIBIT 4

Chronic Toxicity of FD&C Red No. 32 in Rats

(1940)

Method: Five male and 5 female rats were fed a ground commercial animal diet to which 0.1% FD&C Red No. 32 was added. Four male and 6 female rats which received the basic diet served as controls. The rats were 21 or 22 days old at the start of the experiment and weighed from 28 to 51 grams. They were housed in individual cages, given free access to food and water, and were weighed at weekly intervals.

Results: As shown in Table 1 0.1% FD&C Red No. 32 markedly depressed the growth of the rats and reduced

[fol. 401] the median survival time. The last of the rats receiving the color was sacrificed in poor condition in the 58th week, while 7 of the 10 control rats survived to the end of the experiment (101 or 102 weeks).

Table 1

**Weight and Mortality of Rats Fed a Diet Containing
FD&C Red No. 32**

Dosage	Sex	No. of Rats	Weight, gm.		Median Survival Time, Weeks
			Initial	9 weeks	
0%	M	4	39	365	101
	F	5*	33	216	
0.1%	M	5	37	209	17
	F	5	34	121	

* Data sheet on one female rat is missing.

Department of Health, Education and Welfare.

Exhibit No. 4.

Hearing FDC-60.

Offered by: Government.

Date 1/19/54.

Reporter WB.

**[fol. 402] Chronic Toxicity of FD&C Red No. 32 in Rats
(1941)**

Method: Nine male and 11 female rats, 21 or 22 days old and ranging in weight from 33 to 55 grams, were fed a ground commercial laboratory diet containing 0.1 FD&C Red No. 32. The rats were housed in individual cages, given free access to food and water, and were weighed at weekly intervals.

Results: As shown in Table 1, 0.1% FD&C Red No. 32 retarded the growth of these rats as compared with that commonly found in our laboratory on normal diet. The median survival time was 38 weeks. Of the 20 rats, 5 were found dead at intervals from the 18th to the 25th week, 12 were sacrificed because of poor condition at intervals from the 20th to the 71st week, and 3 were sacrificed to terminate the experiment at the 77th or 79th week.

Table 1

Weight of Rats Fed a Diet Containing FD&C Red No. 32

Dosage	Sex	No. of Rats	Weight, gm.	
			Initial	8 weeks
0.1%	M	9	41	170
	F	11	42	145

Pathological Examination of Rats Fed FD&C Red No. 32, 0.1%

Gross and microscopic pathological examination was made of 10 treated animals from the two preceding experiments, and of 5 of their controls, with only gross examination being made of 1 more treated animal and 4 more [fol. 403] controls. The test rats had been on the experiment for 11 to 56 weeks, and the controls from 46 weeks to 2 years. The liver was definitely affected in the test as compared to the control rats, both grossly and microscopically. Grossly, the control livers showed no abnormalities, whereas 7 of the 11 treated ones showed either or both of varying degrees of a tan or nutmeg appearance, or in 1 instance was slightly rough. One of the 7 showed several nodules up to 7 x 7 x 5 mm. Microscopically, the total changes in the 5 controls examined were 1 instance of slight diffuse atrophy and 1 of slight hepatitis. In the 10 treated animals there were, by contrast, 6 instances of slight or moderate bile duct proliferation, 3 of slight hepatic cell hyperplasia irregularly mixed with areas of atrophy, 3 instances of moderate or marked centrilobular hepatic cell necrosis, 1 instance of hepatic cell hyperplasia which in places took the form of adenomatoid nodules mentioned in the gross description, and 1 instance each of slight and moderate fatty change. All 7 instances of hyperplasia and necrosis were in different animals.

Subacute Oral Toxicity of FD&C Red No. 32 in Rats

(1951)

Method: FD&C Red No. 32 was fed at various levels in a basic diet in an effort to determine this maximum tolerated dose. Five weanling male rats weighing 40 to 50 grams (average weight 45 gms.) were fed 2.0% FD&C Red No. 32 and 5 (average weight 46 gms.) were fed 1%. Five more

weanling males (average weight 47.9 gms.) were fed 0.5% FD&C Red No. 32. Later an additional 5 male rats several [fol. 404] days after weaning, weighing between 60 and 70 grams (average weight 65 gms.) were fed 0.5%. A fifth group (average weight 61 grams) was fed 0.25% FD&C Red No. 30 for 10 weeks.

Results: Rats fed at 2% died within 7 days. Those fed at 1% died within 12 days. Weanlings fed at 0.5% died within 21 days. Of the 5 slightly older rats fed 0.5%, 3 died within 26 days and the other two were sacrificed since weight was decreased below starting weight. Of the 5 rats fed 0.25% FD&C Red No. 32, 3 survived for 10 weeks and were sacrificed; 2 died at 7 and 6 weeks respectively.

Chronic Toxicity of FD&C Red No. 32 in Rats (1952)

Methods: Groups of 24 weanling rats of our laboratory strain (Osborne-Mendel) were fed levels of 0.25% and 0.1% of FD&C Red No. 32 in a basic diet of commercial ground laboratory feed. Equal numbers of males and females weighing between 40 and 50 grams were used in each group. Two groups, a total of 48 rats, were fed 0.25% of the color with the expectation that one of these groups could later be raised to a higher level. A third group received 0.1% of the color and the final group, which served as a control, was fed the basic diet. All animals were kept in individual raised cages and allowed free access to food and water. Animal weights and food intake were recorded weekly. Animals found dead but in good condition were opened for observation of gross pathology.

[fol. 405] Results: Inspection of average weight gains recorded in table 1 shows that FD&C Red No. 32 markedly retarded growth of rats at both levels fed. Mortality was strikingly increased at both levels in that all animals fed 0.25% were dead by the 20th week and 16 of 24 animals fed 0.1% were dead by the 26th week. Eight of the control animals are now living at the 100th week of the experiment. The intended raise of the color concentration in one group of 24 animals to a level higher than 0.25% was shown not to be feasible.

Of the 48 animals fed 0.25% 19 showed at autopsy liver damage or enlarged bile ducts or both. Their blood ap-

peared pale and watery. As a group they presented a picture of severe emaciation with complete absence of fat in carcass and viscera. Twelve of 24 animals fed 0.1% showed at autopsy large quantities of fluid in the chest cavity and presented a picture of emaciation and anemia.

The average values for hemoglobin and red blood cell counts taken on survivors at the 18th week of the experiment are shown in table 2 and bear out the general picture of severe to moderate anemia in the test animals as compared to the average of 10 animals of the control group.

[fol. 406]

Table 1

Weight and Mortality of Rats Fed Diets Containing
FD&C Red No. 32

Dosage	Sex	Start		3 Months			12 Months			Months Surviv- ality
		No. of Rats	Avg. Wgt.	No. of Rats	Avg. Wgt.	Wgt. Gain	No. of Rats	Avg. Wgt.	Wgt. Gain	
0%	M	12	46	12	386	340	12	505	459	0
	F	12	46	12	232	186	12	305	259	0
0.25%	M	34	46	13	120	74	0	—	—	100%
	F	34	45	11	103	57	0	—	—	100%
0.1%	M	12	45	10	256	211	2	350	305	75%
	F	12	44	11	174	130	2	195	151	58%

Table 2

Blood Changes in Rats Fed Diets Containing FD&C Red
No. 32 (18 weeks on experiment).

Dosage	No. of Animals	Hemoglobin gm./100 ml.	Red Cells per mm ³	White Cells per mm ³
0.25%	15	9.5	4,000,000	23,000
0.1%	10	12.3	7,450,000	24,500
0%	10	15.22	9,270,000	13,800

Pathological Changes in Rats from Feeding of FD&C
Red No. 32

In the experiment for which the pathological changes are given in this paper, 48 weanling rats of both sexes were started on 0.25% of FD&C Red No. 32 (Oil Red X) in their diet. 24 others were put on 0.10%, and an additional 24 served as controls both for this dye and [fol. 407] for FD&C Red No. 4 (Ponceau SX). The rat numbers were 3991-4086, and the pathology numbers were 14770 for the first rat received and 16810 for the last.

Because of the relatively early deaths of most of the treated animals, not all were sent to the pathology laboratory. There were received 26 of the 48 on 0.25%, all of these 26 having died (20) or been sacrificed because of poor condition (6) after from 9 to 19 weeks of dye feeding. Of the 24 rats started on 0.10% of dye, 14 (8 found dead, 6 sacrificed because of poor condition) were received in the pathology laboratory after from 8 to 89 weeks' feeding; all but 3 of these 14 had been fed for 28 or fewer weeks, the 3 exceptions all being females that survived 51, 72 and 89 weeks respectively. No treated animals are still alive. Of the 24 controls, 8 are still alive at this writing (1-12-54), and of those not surviving, 1 found dead and 7 sacrificed because of poor condition have been received, after from 76 to 96 weeks on the experiment.

Cross Pathology

This portion of the pathological examination is, as customary, based on examination of the viscera fixed in 10% formalin before being sent to the pathology laboratory. In this instance the viscera were en bloc except for most of the older animals, in which they had been more or less cut apart. Rats fed 0.25% dye—The visceral masses were uniformly small for the ages of the animals, varying from slightly to markedly so, and on the whole were somewhat pale, the liver usually showing this best. Smallness of the individual organs was most apparent in [fol. 408] the case of the testes. The liver was not distinctly small. Five livers showed from very slight to slight-moderate roughness of the surface; one of these and 4 others showed very slight to moderate degrees of either a mottled or nutmeg appearance. The common bile duct was consistently enlarged; i.e., its diameter was greater than normal. Of the 26 ducts, one about 3 mm. in diameter was graded as markedly enlarged, 8 with a diameter of about 2 mm. were considered moderately enlarged, 2 were slightly to moderately enlarged (diameter about $1\frac{1}{2}$ mm.), 6 were slightly enlarged (1 to $1\frac{1}{2}$ mm.), 4 were questionably enlarged, and 5 were of normal diameter, not quite 1 mm. rats showed pneumonia in one form or

another, in one instance with pleuropericardial adhesions.

The rats fed 1.10% of the dye showed small and pale viscera, but to a lesser degree than at 0.25% Testicular atrophy varied from none to much. The liver was not disproportionate in size to the rest of the viscera, except for being small in the 2 oldest animals received. Six of the 14 livers had slightly rough surfaces, and 8 had a slight to marked degree of nutmeg appearance. None of the common bile ducts were enlarged, in contrast to the 0.25% group. However, again in contrast to the 0.25% group, in which no cardiac lesions were noted except for the one instance of pleuropericardial adhesions mentioned, nearly all of the animals on 0.10% showed one or more cardiac changes, the most common being right ventricular hypertrophy. This hypertrophy was present in 12 of the 14 hearts; one heart was not received, and that of the longest surviving animal was normal. The degree of the hypertrophy was slight in 5 and more [fol. 409] pronounced in 7 instances; 2 of the slight degrees were combined with dilation of the right ventricle. Enlargement of the right strium up to several times its usual volume was noted 7 times; whitish mural thrombi, whose average size was about that of a match head, were seen in the right ventricle of 4 hearts. Three rats showed pneumonia, 2 of these also having adhesions between lungs and heart.

The control rats, it should be remembered, were on the average much older than the treated animals, and therefore would normally show more of the usual spontaneous lesions that occur with advancing age in rats. Enlarged and granular kidneys were absent in the treated groups, but occurred in 4 of the 8 controls. Four livers showed a slight or moderate degree of nutmeg appearance, and one of these had a slightly rough surface and was very slightly enlarged; of the remaining 4 livers, 1 was slightly enlarged and 2 were slightly small. Only one heart was abnormal; its right strium was slightly and the right ventricle moderately dilated; hypertrophy could not be made out. Three animals had pneumonia. Three had tumors; these were respectively pulmonary lymphosarcoma 1.6 x 0.7 x 0.7 cm.; perioscal lymphosarcoma 4½ x 3 x 2 cm.;

tumor in much of an 8 x 7 x 6 mm. adrenal; this last animal also having a 2 x 1½ x 1 cm. left tube-ovarian chronic abscess. The males had slight or moderate testicular atrophy.

Microscopic Examination

Of the 48 rats received, 29 were examined microscopically, 14 in detail and 15 with attention to only the major [fol. 410] structures of interest. The detailed list included lung, heart, liver, spleen, pancreas, stomach, small intestine, colon, kidney, adrenal, testis (or uterus and ovary), leg bones and bone marrow. All of the foregoing were sectioned for each of the 12 mentioned rats except that one leg was not received. In addition, sections for these 14 rats included 10 urinary bladders, 7 thyroids, 6 prostates, and 3 parathyroids. For the remaining 15 animals, sections included liver, kidney, heart, (in controls) lung, (in males) testis, and occasionally other structures such as tumor, etc. All the foregoing were hematoxylin-cosin stained paraffin sections. In addition, one liver was stained with periodic acid-Schiff and silver stains. The 29 sectioned animals included all 8 controls, 12 of the 14 on 0.10% dye, and 9 representative rats on 0.25%.

Liver: The livers of the treated animals showed a large number of changes which together made up a picture of, in every instance, moderate or marked liver damage in the 0.25% group, and very slight to moderate damage in the 0.10% group. It is difficult to give this process a single exact name. "Moderate to marked subacute degeneration" seems most applicable for the high dose animals, and "mild subacute degeneration and/or cirrhosis" for the low dose animals. The individual changes making up the composite lesion were enlarged, irregular hepatic cells, often in pseudoacinar formation; disorganization of the normal architecture; fibrosis; slight necrosis; increased variability of hepatic cell size; slight nonnuclear and less polymorphonuclear cellular infiltration; very slight bile duct proliferation; and, occasionally rounded nodules of hepatic cells with a proliferative appearance. The necrosis was of a [fol. 411] "nibbling" type, i.e., single cells or small clusters were affected, and not large clumps; also, the degree was probably underestimated at times when obscured by post mortem autolytic changes. The hepatic lesion in the 0.10%

animals was in part a reduction in degree of that in the 0.21% group, and in part it had a different appearance because of the following modifications. The pseudoacinar formations disappeared. Fibrosis was nearly as pronounced, but was concentrated in the centrolobular areas instead of being more diffuse. The occasional foci with a proliferative tendency were absent. The centrolobular areas tended to become a mixture of capillaries, cellular infiltrate, loose fibrous tissue, and necrotic and dropping out hepatic cells; in other words, it could to some extent be called a centrolobular cirrhosis. (Cirrhosis in the rat liver is not exclusively portal; see Ashburn et al., *An. J. Path.*, 23, 159, 1947). Two of the enlarged common bile ducts were sectioned and showed some epithelial proliferation.

The control livers showed 3 exceptional items, each in a different liver. These were (1) slight to moderate bile duct proliferation with preductal fibrosis, (2) metastatic lymphosarcoma cells in the sinusoids, and (3) an appearance not described in detail here but rather often seen in mouse livers and suggestive of chronic or residual hepatitis. Along with the first of these was moderate irregularity of architecture and moderate fatty change. In addition, because of the greater age of the control as compared to the treated animals, there were often seen the common slight liver changes of old rats. (In the following discussion, the previously mentioned unusual items are not considered. For example, there was as much bile duct proliferation [fol. 412] in the control as in the treated rats, but it should be remembered that bile duct proliferation is practically never seen spontaneously in animals of the ages of the treated ones, and that in any event bile duct proliferation was a relatively minor feature of the hepatic lesion caused by dye feeding. Hepatic cell vacuolation interpreted as fatty change was of the same very slight degree throughout the different groups, but this is not considered a part of the changes caused by the dye. Very slight degrees of disarrangement of the normal architecture and of increased variability of cell size were present, as is often seen in old rats, whereas in the treated animals where these changes should have been even less noticeable they were much more pronounced, and were significant parts of the lesion. The important factors of large irregular hepatic cells, pseudo-

acinar formation, necrosis, and fibrosis with associated slight cellular infiltration, all significant parts of the lesion, were not present at all in the 8 controls with the exception of the 1 instance of a different sort of fibrosis as already mentioned.

Heart: With respect to the rats fed 0.10% dye, not a great deal can be added to what has been said under Gross Pathology. Of the 12 hearts grossly showing right ventricular hypertrophy, 11 were sectioned. In those, hypertrophy of the right ventricle was graded as moderate in 7, slight-moderate in 2, slight in 2. In addition to the 4 right ventricular thrombi noted grossly, 2 smaller ones in the same location were seen in the microscopic sections. (Apical clotted blood is not picked out at gross examination for fear of dislodging such thrombi.) All 6 thrombi showed more or less organization and calcification. The right [fol. 413] strium showed hypertrophy as well as dilation. No left ventricular or atrial hypertrophy was seen. Myocarditis and myocardial fibrosis were present in 6 hearts in slight or very slight degree except for one heart in which the process was severe. It was more pronounced in the right than on the left. Since the valves are cut less consistently than the other structures, no exact figures can be given for the valvular thickening with low grade inflammation which was seen in a few hearts; it affected the right A-V valve most, then the left A-V, and apparently not the others. Pericarditis accompanied the 2 instances of pleuro-pericardial adhesions.

In the 0.24% animals, all 9 hearts sectioned were normal except for pericarditis accompanying pleuropericardial adhesions in one instance, and for pyemic foci in another animal in which several organs were so involved. Neither of these can be considered as an effect of the dye. In the controls, the 8 sectioned hearts were as would be expected in a group of this age; there were 3 instances of slight or very slight myocardial fibrosis and myocarditis, all on the left; one of these also showed slight left ventricular and atrial hypertrophy; an additional heart (from the animal with the peculiar bile duct proliferation) showed very slight thickening of both A-V valves. No rightsided lesions were seen.

Spleen: The spleen in rats fed 0.25% dye showed, generally speaking, slight lymphoid atrophy together with

slight myelosis; at 0.10% dye 5 of the 6 sectioned showed slight hyperplasia, more erythroid than otherwise, while the spleen of the oldest animal was moderately atrophic, [fol. 414] with much pigment (its bone marrow was not sectioned).

Bone Marrow: The bone marrow showed very little change at 0.10%; at 0.25% moderate depletion was present in 2 of the 7 sectioned; 1 of this pair and 2 others showed a certain amount of "left shift."

Other Structures: In the controls, the 3 tumors were as mentioned under Gross Pathology, with the additional notation that the adrenal tumor was cortical in type. The enlarged and granular control kidneys showed the usual type of chronic nephritis seen in our old rats; and did not show the slight changes of another type seen in the treated rats and to be mentioned later. The pneumonias in the controls were of the usual chronic type, while those in the treated rats were more acute and of a necrotising type, with masses of bacteria. The epiphyseal lines in the leg bones of both treated groups were narrowed (markedly at 0.21%, moderately at 0.10%, showing reduced bone growth, in all probability a secondary effect through inanition rather than a direct effect of the dye. The testes in both treated groups, showed from little to much atrophy (normally, males of their ages show essentially no atrophy), and the much older controls showed from no to moderate atrophy. Because of its variability in degree, the atrophy in the treated animals is considered an indirect (inanition) effect. In each treated group, 3 kidneys showed small amounts of brown tubular epithelial pigment of the wear-and-tear type, and 3 in the 0.25% group showed slight vacuolation of the tubular epithelium; these mild changes are also considered indirect. The uteri in the 0.25% group were atrophic. Any [fol. 415] organs sectioned and not mentioned showed nothing attributable directly to the dye, no incidental changes of any consequence, and sometimes minor degrees of inanition changes.

Summary and Conclusions

Of 48 rats of both sexes started at weaning on the feeding of 0.25% of FD&C Red No. 32 (Oil Red XO) in their diet, 26 were received in the pathology laboratory after from 9

to 19 weeks of dye feeding. Similarly, of 24 rats on 0.10% of dye, 14 were received after 8 to 89 weeks (usually not over 28 weeks) of feeding. None of the treated animals was alive at this writing. Of 24 control rats, 8 are still alive, and 8 others have been received after 76 to 96 weeks on the experiment. "Received" refers to the mass of viscera, generally en bloc, fixed in 10% formalin.

On gross examination, the rats fed either level of dye showed small and pale viscera, more so at the higher level. The liver, however, was not distinctly altered in size. In both groups some livers showed slight roughness of the surface, and varying degrees of a nutmeg appearance. At the 0.25% level, the majority of the common bile ducts were enlarged in diameter, whereas at 0.10% none were. Contrariwise, the heart showed no lesions in the 0.25% animals, and only one instance of dilation in the controls, whereas almost every animal in the 0.10% group showed right-sided cardiac changes, namely one or more of ventricular hypertrophy, ventricular thrombosis, or atrial enlargement. Certain changes occurred in the controls; because of their much greater age, that did not occur in the treated animals; [fol. 416] these are given in detail in the text. Both control and treated animals showed scattered instances of pneumonia.

Microscopic examination in greater or lesser detail was done on 29 of the 48 rats received, including all 8 controls, 12 of the 14 on 0.10% dye, and 9 animals representative of those on 0.25% dye. Microscopic liver changes were much more striking than the gross appearance, particularly at the higher level of feeding. Every one of the 9 sectioned animals on 0.25% dye showed a moderate or marked degree of a process which is difficult to name precisely but which can best be called "moderate to marked subacute degeneration," whose individual factors were large irregularly shaped hepatic cells, pseudescinar formations, disorganization of the normal architecture, fibrosis, a "nibbling" type of necrosis, and several other items. In the 0.10% rats liver damage varied from very slight to moderate, and it could best be called "mild subacute degeneration and/or cirrhosis." Certain histological differences between the livers of the two groups are given. Microscopically, the hearts of the 0.25% animals showed nothing

attributable to the dye feeding, whereas in the 0.10% group the microscopic examination was simply a repetition of the gross picture, showing a constant effect of the dye feeding on the heart. Changes in various other organs were sometimes pronounced, but were for the most part attributable to inanition. In the controls, certain changes occurring principally because of advanced age are discussed; these changes were not confusing in the evaluation of changes caused by the dye.

[fol. 417] Conclusion: Feeding of 0.25% in the diet of FD&C Red No. 32 to rats caused early death, changes of inanition, and moderate to marked liver damage. Feeding of 0.10% caused less inanition, allowed somewhat longer but still short life, caused very slight to moderate liver damage, and caused one or more lesions in nearly every heart examined.

Test of FD&C Red No. 32 for Carcinogenicity by Repeated Subcutaneous Injection Into Rats

(1953)

1. First Experiment

Method: Thirty-six comparable rats (Osborne Mendel) were divided into 2 groups of 18, each group being comprised of 9 males and 9 females. The 36 rats had the following litter-mate arrangement: 4 rats (2 male, 2 female) from each of 9 litters were so divided that 1 male and 1 female from each litter-mate group was injected with either FD&C Red No. 32 suspended in glycerine or with glycerine alone.

The injections were made weekly. The FD&C Red No. 32 was suspended in 5% W/W concentration in glycerin. The control rats each received the same volume of glycerin per week as did the individual Red 32 rats. All surviving Red 32 animals received a total of 8 weekly injections as follows: 0.1 cc glycerine (containing approx. 5 milligrams of Red 32) for each of the first 2 weeks, 0.15 cc for the 3rd week, and 0.2 cc for each of the last 5 weeks.

Results: Of the rats which received FD&C Red No. 32 one died after 7 injections, 4 died and 2 were sacrificed [fol. 418] in extremis after 8 injections. There were no fatalities among the control animals. The injections were discontinued at this time and all animals were sacrificed

a few weeks later. Toxic symptoms and findings observed in the animals which received FD&C Red No. 32 included lethargy, paleness of the animal, hemorrhage, and reduction in the size of the liver. The results of blood counts which were taken are given in Table 1 and show anemia in the experimental animals. Since the experiment had to be cut short because of toxic effects, there was no opportunity to evaluate the possible carcinogenic action of the color and a second experiment was set up.

Table 1.

Blood Counts on Rats Injected With FD&C Red No. 32

	FD&C Red No. 32	Control
5 weeks		
Hemoglobin, gm/100 ml.....	11.9 (5)*	15.5 (5)
Red Cells per mm ³	6,100,000 (5)	8,500,000 (5)
White Cells per mm ³	14,400 (5)	17,800 (5)
8 weeks		
Hemoglobin.....	7.9 (5)	15.5 (5)
Red Cells.....	4,600,000 (5)	9,800,000 (5)
White Cells.....	19,900 (5)	16,900 (5)
9 weeks		
Hemoglobin.....	11.1 (10)	
Red Cells.....	8,300,000 (9)	
White Cells.....	18,300 (9)	

* Figures in parentheses are the number of animals represented in the average shown.

[fol. 419] Second Experiment.

Method: In this experiment two groups of 18 rats, equally divided as to sex, were injected subcutaneously at weekly intervals with 0.1 cc. of a 1% (w/w) suspension of FD&C Red No. 32 in glycerin, and glycerin respectively. The rats were so distributed that one male and one female from each litter are represented in the control and the experimental group. A similar experiment on FD&C Orange No. 2 was conducted in parallel with this experiment and the same control animals served for the two colors.

Results: Because of adverse effects observed in the FD&C Orange No. 2 rats this experiment was also discontinued after 8 injections. In the case of the FD&C Red No. 32 rats there was no significant effect on growth, and no changes were observed at the injection sites.

Carcinogenicity Tests in Mice With FD&C Red No. 32 (1940)

The color was made into a glycerin paste and inserted by means of a modified trocar into the right axillary region subcutaneously of eighteen C57 black mice (10 males and 8 females [271-288]) and 18 swiss white mice (18 males [21'-270]). Each mouse received 10.8 milligrams of the color each injection. The first injection was made on 10-17-40 and 10-14-40 for the two groups respectively and repeated 6, 18, 23, and 35 weeks thereafter with the swiss group also receiving an injection 47 weeks after the first.

No tumors were seen at autopsy by gross examination. [fol. 420] A similar set of control mice was injected with the amount of glycerin used to make the paste at approximately the same periods.

Chronic Toxicity of FD&C Red No. 32 in Dogs (1938-1944)

Method: In this experiment the dogs received the FD&C Red No. 32 dissolved in corn oil and administered in gelatin capsules, daily except Sunday. One male and 4 females received 5 mg. per kg. of body weight per day for 64 to 73 months. One of these females had previously received 100 mg. per kg. per day for 36 days, and 20 mg. per kg. per day for 27 days. One male dog received 100 mg. per kg. per day for about 10 months and after a month's rest received 20 mg. per kg. per day for 60 months. One of the constituents of FD&C Red No. 32, the paraisomer, was administered to 2 dogs at a dose of 5 mg. per kg. per day for 72 months. Another constituent, the meta isomer, was administered to 3 dogs at a dose of 5 mg. per kg. per day for 72 months.

Results: No adverse effects were noted during the experiment which could definitely be attributed to the color except during the period that the 2 dogs received 100 mg. per kg. per day. At this dosage there was observed moderate weight loss which was subsequently regained when this dosage was discontinued or reduced. All dogs were sacrificed at the end of 5 or 6 years on the dosage detailed under "Method."

All eleven dogs were examined grossly and microscopically. As is usual in dogs of their age, they consistently [fol. 421] showed varying numbers of splenic lymphomatosus nodules, and a few had old splenic capsular hemorrhage, another age change. The dogs had heartworms and one pneumonia. The only tumor was an 8 mm. fibrous mass projecting from the surface of the jejunum. Two dogs had renal cysts, 5 and 8 mm. respectively. From each of these dogs microscopic sections were made of lung, heart, liver, gall bladder, spleen, pancreas, mesenteric lymph nodes, stomach (or duodenum), small intestine, colon, kidney, adrenal, urinary bladder, testis (or ovary), prostate (or uterus), thyroid and parathyroid. All these microscopic sections showed nothing unusual except for the tumor, diagnosed as probably an argentaffinoma, and not attributable to treatment. A number of minor changes were seen in various organs; these together with the gross changes noted were considered to be within the limits of what might normally be expected in a group of dogs of this age, and it was concluded that there was no effect from treatment.

Chronic Toxicity of FD&C Red No. 32 in Dogs

(1953)

Method: This dye was fed at levels of 0.2%, 0.4%, and 0.1% in a basic diet of ground laboratory chow. Each dog was housed in an individual metabolism cage, was fed and watered daily and had free access to his food. Each dog was weighed approximately weekly. A total of 7 females and 3 males was used.

Results: The four dogs which were started at 0.2% FD&C Red No. 32 in their diet ate poorly and two were sacrificed [fol. 422] in poor condition at 26 days after having lost respectively 28% and 29% of their initial weight. The remaining two, which had lost respectively 24% and 19% were placed on a control diet for about 10 days. During this time they regained some weight and improved their physical condition. Along with two additional dogs they were placed on a diet of 0.01% FD&C Red No. 32. One of these four dogs lost about 60% of its body weight and was found dead after 173 days on the 0.01% diet. The remaining three have lost some weight but appear in fair condition after nearly 10 months on this level. All four of

the dogs on the intermediate level, 0.04%, were sacrificed in extremis at 124, 137, 148, and 148 days respectively. All had lost about 50% of their body weight. Sporadic but not severe diarrhea was observed during the experiment.

Pathological Changes in Dogs from Feeding of FD&C

Red. No. 32

Path No.	Dog No.	Sex	Appr. Age, No.	% Dye in Diet	Days on Expt.	F.D.** or K.	Weight in Kg.	
							Beg.	End
15708	D-123	F	36	0.20	26	K.	14.2	10.1
15709	105-261	M	10	0.20	26	K.	9.3	6.7
16077	M-302-a	M	15	0.04	124	K.	12.8	6.4
16120	M-302-1	F	16	0.04	137	K.	10.7	4.9
16299	98-240-a	F	63	0.04	148	K.	12.2	6.6
16300	105-262	M	12	0.04	148	K.	10.6	5.6
16376	M-277	F	53	0.01*	173*	F.D.	7.4	2.9

* After 1 month on 0.20%; weight during that month dropped from 8.8 to 6.7 kg.

** F.D. = found dead; K. = sacrificed because of poor condition.

[fol. 423]

Cross Pathology

15708—Slight to moderate emaciation; very little body fat. Skin slightly dirty. Liver has slight orange-red tinge, but otherwise appears normal. Spleen pale red; bloodless. Slight-moderate yellowish radial streaking of renal cortices. No worms seen in this or any of the following dogs; cecum included.

15709—Little emaciation; some body fat. Liver slightly pale and tan. Gall bladder moderately contracted; bile dark green and gelatinous. Mesenteric and cervical lymph nodes moderately enlarged. External appearance (skin, eyes, nose, pads) plus interior of mouth normal on this and following dogs.

16077—Marked emaciation; slight dehydration. Liver slightly-moderately atrophic; firm; slightly pale and tan. Moderate amount of thick, dark bile in gall bladder. Intestinal contents normal in amount and consistency, but dark green-black in color. After fixation, stomach mucosa shows moderate number of superficial 1-2 mm. ulcerations. Bone marrow gelatinous.

16120—Marked to extreme emaciation. Tissues in general appear slightly anemic. Liver slightly atrophic; firm; dark reddish tan color. Stomach contains moderate amount

of watery coffee-ground material; mucosa appears normal. Feces brown-black. Bone marrow gelatinous (stringy), pale. Kidneys dark tan color.

16299—Moderate to marked emaciation. Liver and kidneys slightly pale and tan. Spleen shows moderate [fol. 424] amount of old capsular hemorrhage. Bone marrow slightly gelatinous.

16300—Marked to extreme emaciation. Liver slightly atrophic, pale, and tan. Gall bladder bile dark and viscid. Spleen pale red. Tissues in general slightly-moderately anemic.

16376—Extreme emaciation, slight dehydration; tissues appear anemic. Marked post mortem autolysis. Liver dark red-brown. Spleen pale red. Bone marrow slightly gelatinous.

Microscopic Pathology

Because of post mortem autolysis, microscopic examination of 16376 was limited to liver, kidney and bone marrow, including fat stains and smear respectively. From each of the remaining 6 dogs, homstoxylin sosin stained paraffin sections of formalin-fixed tissues were made from lung, heart, liver, gall bladder, spleen, pancreas, lymph nodes, kidney, adrenal, stomach (2), small intestine (3), colon, thyroid, parathyroid (except 16120), urinary bladder, voluntary muscle, testis (or ovary), uterus (or prostate, except 16300, lost), submaxillary salivary gland, and rib bone and marrow; also, from each of these 6 dogs frozen sections of liver and kidney were stained for fat with Oil Red O, a smear of bone marrow was stained with Giemsa type stain, and paraffin sections were made of liver and kidney fixed in Zenker's fluid. Some adrenals were also stained for fat and/or had portions fixed in Zenker's fluid. All of these sections were normal or essentially so except as follows.

[fol. 425] Atrophic Changes in Various Organs: This was the basic pathological pattern. For convenience, the most consistent and easily graded of these changes are shown in tabular form, and the degree of bodily emaciation is repeated. In the table, 1—slight, 2—moderate, 3—marked or severe, and 4—extreme. The changes in the bone marrow, and to a lesser extent in the spleen and lymph nodes, are a depletion of certain cells rather

than actual shrinkage in size of the organ or of its component cells, but the term atrophy is often used and generally understood, and for convenience it is used here. In the skeletal muscles, there were changes (nuclear multiplication, necrobiosis, necrosis) in addition to the atrophy, so that the total muscle lesion is a dystrophy rather than simple atrophy. Of the organs not listed, atrophic changes in the ovary and uterus were the most common.

The figures in the table have no mathematical exactness for comparative purposes because of subjective factors, differences in the atrophic process among various organs, and the difference between depletion and atrophy mentioned above. Because of the great liability of the bone marrow, a few words of explanation about it may help. Our dog rib marrow, on the average, normally are made up of (by inspection, not measurement) about 1/3 hematopoietic (plus a small percentage of stroma) cells, about 1/2 fat cells, and the remainder by, chiefly, capillary blood vessels. In determining these values the artefacts of shrinkage spaces, and the relative unobtrusiveness of fat cells in routine paraffin sections have been considered. The moderate bone marrow depletion shown in the table means a reduction in hematopoietic cells of around 50% of the normal.

[fol. 426]

Pathology No.	Bodily Emaciation	Degree of Atrophic Changes						
		Liver	Spl.	Lym.N.	Mär.	Test.	Pro.	Muscle
15708	1-2	±	0	0	0	Fem.	Fem.	0
15709	1	0	0	0	0	1-2	2	1
16077	3	3	2	1	2	2	2	1
16120	3-4	2-3	2	2	2	Fem.	Fem.	2-3
16299	2-3	1	1	1-2	2	Fem.	Fem.	±
16300	3-4	2	2	1-2	2	3	Lost	2
16376	4	2-3	N.S.	N.S.	±	Fem.	Fem.	N.S.

Abbreviations in last 6 columns mean respectively, Spleen, Lymph Nodes, Marrow, Testis, Prostate, Female, and Not Sectioned.

Changes Other than Atrophy and/or Cellular Depletion: Fatty change in the liver was slight. Some times our supposedly normal dogs show a very small amount of stainable liver fat. Five of the present lot showed a very small amount, 15709 showed a slight degree of fatty change, and 16376 (the animal found dead) a slight to moderate degree. In the kidney, normally present fat

(in other laboratories as well as our own) has a wider variation in amount, and the present group of dogs was not outside this normal range of variation. In the stomach, 16120 and 16299 showed slight ballooning (enlargement and rarefaction) of the fundic parietal cells; 16077 showed small foci of recent mucosal necrosis. In the bone marrow, the myeloid/erythroid ratio was determined only by inspection, not counting. In the first dog in the table it appeared slightly increased; in the remainder it was not definitely abnormal, although the gelatinous nature of the majority of the marrows interfered with obtaining [fol. 427] well-stained smears. Hemosiderin in the bone marrow and liver varied from none to moderate in amount; the animals showing the most of this pigment were 16299 and 16376. Certain changes in the skeletal muscles were previously mentioned; both these and the atrophy were greater in the thigh than in the neck, the 2 muscle sites routinely sectioned. Frank necrosis was not prominent, but nuclear multiplication and necrobiosis more or less paralleled the atrophy.

Except for the single bone marrow, the positive findings mentioned in the above paragraph can be attributed to treatment, as, of course, are the atrophic previously mentioned. Certain other changes, scattered among the various organs and none of major proportions, cannot be attributed to treatment.

Summary and Conclusions

Cross and microscopic pathological examination has been made of 7 dogs fed FD&C Red No. 32 (Oil Red XO) at dosage levels of from 0.01% to 0.20% of the diet for periods of 26 to about 200 days. One dog was found dead and the others sacrificed because of their poor condition.

On gross examination, the only external change of significance was consistent emaciation, usually pronounced and varying from slight to extreme. Internally, the common changes were slight or moderate pallor (anemia) of the organs and tissues in general, gelatinous bone marrow, and atrophy of the liver. No worms were found.

[fol. 428] Detailed microscopic examination was done on 6 of the 7 dogs, and some on the remaining one. The microscopic picture was consistent, the basic pattern being

that of atrophy and/or cellular depletion in various organs, the most frequently affected being liver, spleen, lymph nodes, bone marrow, genital organs, and skeletal muscle. In general, these atrophies paralleled the degree of emaciation. In addition, the changes attributable to treatment included slight fatty change in the liver; slight changes in some stomach, dystrophic changes in skeletal muscle in addition to the atrophy, and a certain amount of hemosiderosis of liver and bone marrow. The changes were greater in those animals fed the low doses for longer periods than in those fed the high dose for shorter periods.

Cathartic Action of FD&C Red No. 32 in Dogs (1952)

Ten of the eleven dogs which had been found to be sensitive to the cathartic action of FD&C Orange No. 1 were tested on FD&C Red No. 32. The dogs were fasted overnight, given a weighed amount of the color in a capsule and then fed two hours later. Of the ten dogs which received a dose of 200 mg. each, eight developed diarrhea. When five of the dogs were later similarly tested at a dose of 100 mg. each, four developed diarrhea and one gave questionable results.

[fol. 429]

EXHIBIT 8.

Table 9. A Summary Table on the Concentration of Dye on Color-Added Oranges and in Products Made from Color-Added Oranges.

Substance	Concentration of dye in ppm
Whole fruit (extraction and chromatographic separation)	3.39—4.69
Whole fruit (chloroform washing)	4.96—6.78
Peel of fresh fruit (extraction and chromatographic separation)	17.63—24.39
Peel of fresh fruit (chloroform washing)	25.79—34.26
Juice	.64—.07
Candied peel	7.4
Marmalade	1.8

[fols. 429 a-b] Clerk's Certificate to foregoing transcript omitted in printing.

[fols. 430-431] IN SUPREME COURT OF THE UNITED STATES,
OCTOBER TERM, 1957

No. —

[Title omitted]

ORDER EXTENDING TIME TO FILE PETITION FOR WRIT OF
CERTIORARI—November 27, 1957

Upon consideration of the application of counsel for petitioner(s),

It is ordered that the time for filing petition for writ of certiorari in the above-entitled cause be, and the same is hereby, extended to and including January 3d, 1958.

Hugo L. Black, Associate Justice of the Supreme Court of the United States.

Dated this 27th day of November 1957.

[fol. 432] IN SUPREME COURT OF THE UNITED STATES,
OCTOBER TERM, 1957

No. 703

MARION B. FOLSOM, Secretary of Health, Education and Welfare, Petitioner,

vs.

FLORIDA CITRUS EXCHANGE, FRANK R. SCHELL, et al.

ORDER ALLOWING CERTIORARI—March 17, 1958

The petition herein for a writ of certiorari to the United States Circuit Court of Appeals for the Fifth Circuit is granted.

And it is further ordered that the duly certified copy of the transcript of the proceedings below which accompanied the petition shall be treated as though filed in response to such writ.